Radiopharmaceutical Dosage Selection for Pediatric Nuclear Medicine

Richard M. Shore and William R. Hendee

Departments of Pediatrics and Radiology, The Children's Hospital and Ohio State University, Columbus, Ohio, and Department of Radiology, University of Colorado Health Sciences Center, Denver, Colorado

To identify the most rational method for adjusting adult radiopharmaceutical dosages for children, four methods of dosage computation were examined from the perspectives of diagnostic adequacy and radiation absorbed dose. For static imaging, information density is the most important factor in study quality, and adjustment of dosage by body weight (Wt) for "thick" organs, and body surface area (BSA) for "thin" organs is recommended. Compared with adults, small children receive less radiation exposure if radiopharmaceutical dosages are adjusted by Wt, and slightly greater exposure if dosages are adjusted by BSA. For dynamic imaging studies, dosage requirements are governed by the spatial resolution needed for region of interest assignment, and the statistical reliability of the time-activity data. For dynamic renal imaging, renograms of similar quality are obtained if dosages are adjusted by height (Ht). Dynamic cardiac studies might appear to require dosages even larger than those adjusted by Ht which would result in higher radiation absorbed doses to pediatric patients. However, smaller dosages can be used in children by prolonging the imaging time and accepting lower temporal resolution. Dosage requirements for dynamic studies depend on which physiologic characteristics are measured from the time-activity data. Since the measurements of some characteristics demand higher count rates than others, dosage requirements ultimately depend on which measurements are clinically necessary. Close attention to the factors that determine these requirements may yield significant reduction in dosages, and thus in radiation exposure, for patients of all ages.

J Nucl Med 27:287–298, 1986

The optimal radiopharmaceutical dosage for a diagnostic study is the least amount that yields a clinically adequate examination.* Of particular interest is the selection of radiopharmaceutical dosages for children. Various methods have been recommended for scaling adult dosages down to levels appropriate for pediatric patients. A previous study documented a wide range of pediatric radiopharmaceutical dosages which were administered at 26 representative hospitals in the United States (*1*). These dosages generally exceeded those which would have been calculated by all of the currently accepted methods, and this was often by a large amount (*1*). More recently, the Pediatric Radiopharmaceutical Dose Subcommittee of The Society of Nuclear Medicine has also called attention to a large variability in the dosages used for pediatric patients, finding tenfold differences between institutions (*2*). Although the amount needed for a study is ultimately determined empirically, the wide variation in administered dosages indicates either disagreement on what constitutes an adequate examination, or inconstant attention to titrating dosages down to the least amount. To help resolve these differences and to assist in developing more uniformly accepted dosage schedules, we believe that it is useful to examine the theoretical factors that should determine the diagnostic adequacy of various approaches to radiopharmaceutical dosage selection. Although considerable effort has been devoted to the computation of radiation absorbed doses for children from nuclear medicine examinations, less attention has been paid to the factors that influence the amount of radioactivity which is needed for a diagnostically adequate study. Mitchell (*3*) and Webster (*4*) have outlined some of the important considerations in arriving at an appropriate dosage for static nuclear

Received Apr. 8, 1985; revision accepted Oct. 28, 1985.

For reprints contact: Richard M. Shore, MD, Dept. of Radiology, The University of Wisconsin, 600 Highland Ave., Madison, WI 53792.

* In this paper "dosage" is used to indicate the amount of a radiopharmaceutical used for a study, and "dose" refers to the energy absorbed in tissue (radiation absorbed dose).

TABLE 1
Body Size and Organ Weights (*5–9*)

Age (yr)	Weight (kg)	Height (cm)	Surface area (m^2)	Liver (g)	Brain (g)	Thyroid (g)	Heart (g)
Newborn	3.4	50.4	0.225	110	372	1	24
1	10.2	75	0.47	300	1,005	2	45
5	18.4	109	0.76	608	1,180	5	90
10	32.2	139	1.10	896	1,355	8.8	160
15	53.0	164	1.56	1,297	1,367	13	235
Adult	70.0	174	1.73	1,809	1,451	20	300

medicine studies in pediatric patients. Our report expands these considerations and extends them to selected dynamic studies, where the factors determining dosage requirements are different than those for static imaging. Also examined are the effects on radiation absorbed dose for different methods of pediatric dosage computation.

The goals of this report are to provide a framework for viewing dosage requirements in patients of various sizes, and to indicate the factors that should be considered in critically evaluating dosage schedules. The conclusions that are reached regarding dosage recommendations are theoretical and have not been clinically demonstrated to be efficacious. Some of the conclusions may be discordant with current clinical practice. Such instances would indicate the need to re-evaluate both the validity of the assumptions presented here, and the possibility that more efficacious and radiation cost effective dosages might be achieved through modification of either the standard "adult dosage" or the method used to compute pediatric dosages.

ASSUMPTIONS AND THEORETICAL INVESTIGATION

Body Size

Typical weights (Wt) and heights (Ht) and body surface areas (BSA) for newborns and children 1, 5, 10, and 15 yr of age are given in Table 1. The Ht and Wt data represent the fiftieth percentile values averaged for boys and girls (*5*). BSA values were determined from Ht and Wt by use of a nomogram modified by West from data of Boyd (*6*). Adult Ht (174 cm) and Wt (70 kg) are those used for the ICRP reference man (*7*). Adult BSA is assumed to be 1.73 m^2 as defined by the ICRP.

Organ Size and Shape

Age specific weights for the brain, liver, and thyroid, included in Table 1, are those used in pediatric phantoms by Poston (*8*). Heart weights are interpolated from Lowery (*9*). It is assumed that organ shape remains constant throughout growth so that cardiac chamber volumes are proportional to heart weight, and fractional surface area and cross-sectional area are given by (fractional weight)$^{2/3}$. It is also assumed that blood volume and extracellular fluid volume (for the distribution of technetium-99m diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA) are linearly proportional to Wt.

Radiation Absorbed Dose

Age specific radiation absorbed doses (mrad/mCi) in Table 2 for target organs and the whole body are from Kereiakes and Rosenstein (*10*) based on work of Kereiakes et al. (*11*) and Roedler et al. (*12*). The whole body dosimetry for Tc-99m red cells is from NCRP Report 73 (*13*).

Radiopharmaceutical Dosages

Typical adult radiopharmaceutical dosages are taken to be: liver-spleen imaging [^{99m}Tc]sulfur colloid-5 mCi, brain imaging [^{99m}Tc]DTPA 20 mCi, thyroid imaging iodine-123 NaI-300 μCi, dynamic renal imaging [^{99m}Tc]DTPA-5 mCi, gated cardiac ventriculography [^{99m}Tc]red cells-25 mCi, and thyroid uptake iodine-131 NaI-5 μCi. The methods used to calculate pediatric dosages included multiplication by: Ht/174 cm (Method 1); BSA/1.73 m^2 (Method 2); Wt/70 kg (Method 3); and (age in years + 1)/(age in years + 7) (Method 4; Webster's rule) (*4*). The multiplication factors determined by these methods are given in Table 3. Although adjustment by Ht is not currently considered an acceptable method of calculating pediatric radiopharmaceutical dosages, it is included not only to illustrate the effects of adjustment by one, two, or three dimensions (Ht, BSA, Wt), but also because it may be a rational method for some dynamic imaging procedures.

Factors Influencing Study Quality

Static imaging studies. In static imaging studies, the size of a detectable lesion depends on intrinsic contrast and the spatial resolution of the imaging process. In nuclear medicine, contrast resolution depends strongly on information density (ID, counts per unit area); with higher ID, smaller differences in relative counts between the lesion and the surrounding tissue can be appreciated. Information density is the principal

TABLE 2
Radiation Absorbed Doses from Radiopharmaceuticals (*10–13*)
(mrad per mCi)

Item	Newborn	Age (yr) 1	5	10	15	Adult
[^{99m}Tc]sulfur colloid						
Liver	2,900	1,300	920	560	400	340
Whole body	140	56	38	27	20	19
[^{99m}Tc]DTPA						
Kidney	390	150	100	68	51	40
Whole body	170	62	43	29	21	16
[^{99m}Tc]red cells						
Whole body	200	70	40	30	20	20
[^{123}I]NaI						
Thyroid (× 10^3)	160	110	51	30	21	13
Whole body	350	130	79	51	45	30
[^{131}I]NaI						
Thyroid (× 10^5)	160	110	52	30	22	13
Whole body	10,000	2,000	1,300	810	530	450

factor influencing the selection of radiopharmaceutical dosages in the pediatric patient (*3,4*). For "thin" organs, such as the thyroid, ID is determined by the amount of radioactivity in the organ divided by the imaged area. For "thick" organs, such as the liver or brain, the detected photons arise primarily from the organ surface, with a diminished contribution of counts from deep within the organ. In this case, ID is determined principally by the activity per gram of tissue near the surface of the imaged organ.

Thyroid imaging. The thyroid is a thin organ that is assumed to have a constant fractional uptake of iodine at all ages, recognizing that uptake is transiently elevated in the immediate neonatal period. If the same imaging distance and time are used for all patients, where MF is the multiplication factor for determining pediatric dosage, and ID_A is the ID for an adult, then the ID_C for a child is

$$ID_C = MF \times \left(\frac{20\ g}{\text{thyroid wt}}\right)^{2/3} \times ID_A.$$

A pinhole collimator provides a magnified view of the thyroid. For small patients, the gland may be positioned close to the pinhole to yield a higher ID. However, if collimator resolution equivalent to that obtained with adult patients is desired for the smaller thyroid, then the pinhole diameter should be reduced by the same factor as the reduction in object distance. In this case, ID will remain constant, but effective spatial resolution is improved by utilizing a larger crystal area.

TABLE 3
Multiplication Factors for Pediatric Radiopharmaceutical Dosage

Method	Newborn	Age (yr) 1	5	10	15	Adult
Method 1; $\frac{Ht}{174\ kg}$	0.2897	0.4310	0.6264	0.7989	0.9425	1
Method 2; $\frac{BSA}{1.73\ m^2}$	0.1301	0.2717	0.4393	0.6358	0.9017	1
Method 3; $\frac{Wt}{70\ kg}$	0.0468	0.1457	0.2629	0.4600	0.7571	1
Method 4; $\frac{Age + 1}{Age + 7}$	0.1429	0.2500	0.5000	0.6471	0.7273	1

Liver-spleen imaging. The liver is a thick organ and the ID_C for a child imaged for the same time as an adult is

$$ID_C = MF \times \frac{1809\ g}{\text{liver wt}} \times ID_A.$$

Brain imaging. Brain imaging differs from thyroid and liver-spleen imaging by the distribution of the radiopharmaceutical. Although only the brain is imaged, all conventional brain imaging agents are distributed throughout the extracellular fluid, which is assumed to be proportional to Wt. Where the ID for an adult is ID_A, the ID_C for a child imaged for the same time is

$$ID_C = MF \times \frac{70\ kg}{Wt} \times ID_A.$$

Counts required. Static images are often acquired with a preselected number of counts. To obtain images of similar ID in patients of varying size, counts need to be adjusted by the relative area imaged, which is expressed as (organ wt/adult organ wt)$^{2/3}$.

Dynamic Imaging Studies

For dynamic imaging studies, an adequate radiopharmaceutical dosage provides images with sufficient spatial resolution to permit unambiguous identification of regions of interest, and time-activity curves with enough counts that they are not unduly influenced by statistical noise. Which of these characteristics is the limiting factor varies with the type of study.

Dynamic renal imaging. In dynamic renal studies, the data can be summed over the first 3–5 min of an examination to produce a composite image with sufficient counts to define regions of interest for the kidneys and background. In these studies, the major limitation to data analysis is not spatial resolution, but the statistical reliability of the renogram curve. Each point on the renogram represents the total number of counts from the region of interest, rather than counts per unit area (ID). Early in a dynamic renal study the amount of activity in the kidney depends on the plasma concentration and clearance, which for [^{99m}Tc]DTPA is the glomerular filtration rate (GFR). With the assumptions that plasma concentration is inversely proportional to Wt, and that the GFR is directly proportional to BSA, where the counts for an adult are C_A, the counts C_C for a child are

$$C_C = MF \times \frac{70\ kg}{Wt} \times \frac{BSA}{1.73\ m^2} \times C_A.$$

Gated cardiac ventriculography. In gated cardiac ventriculography changes in ventricular volume are inferred from changes in ventricular counts. Implicit in this relationship is the assumption that the ventricular blood pool is a "thin organ" and that ventricular counts are proportional to the blood concentration of activity and ventricular volume, rather than ventricular area. The blood volume is assumed to be proportional to Wt, and ventricular volume is assumed to be proportional to cardiac weight. Therefore, where the ID of the left ventricle for an adult is ID_A, the ID_C for a child is

$$ID_C = MF \times \frac{70\ kg}{Wt} \times \left(\frac{\text{heart wt}}{300\ g}\right)^{1/3} \times ID_A.$$

Analysis of gated cardiac studies requires accurate delineation of ventricular edges. In estimating the ejection fraction, any absolute error in edge determination produces a greater relative error in small children than in adults. Since greater spatial resolution is needed in small children, ID may not completely describe the adequacy of study quality across age groups. If the image of a small heart were projected over the same crystal area as that for an adult, then equivalent image quality would require an equal number of counts. With less crystal area used, even an equal number of counts will be associated with poorer resolution relative to heart size because of limitations of the detector system. These considerations imply not only that as many counts need to be acquired for a small heart as a large one, but also that spatial resolution needs to be improved for small hearts, even at the expense of lower sensitivity. Where the number of ventricular counts for an adult is C_A, the counts C_C for a child imaged for the same time are

$$C_C = MF \times \frac{70\ kg}{Wt} \times \frac{\text{heart wt}}{300\ g} \times C_A.$$

Nonimaging Study: Thyroid Uptake

Thyroid uptake estimates require that a sufficient number of counts be obtained for statistically valid measurements. The counting time required for these measurements is related to the activity in the thyroid. If normal thyroid uptake is similar at all ages, a fixed administered dosage would yield an equivalent count rate in all age groups; however, this activity concentrated in a small thyroid would yield excessive radiation doses in children. Therefore, the methods of dose calculation can be compared by their effect on the time needed for the examination, which is inversely related to dosage. Where the time needed to obtain sufficient counts in an adult is T_A, the time T_C required for a child is

$$T_C = \frac{1}{MF} \times T_A.$$

Theoretical Investigation

For each of the studies described, pediatric dosages were calculated by each of the four methods for children ages 0, 1, 5, 10, and 15 yr. The methods of computing dosages were then examined for their effects on study quality and radiation absorbed doses.

TABLE 4
Static Imaging Studies: Relative Information Density

Item	Method	Newborn	Age (yr) 1	5	10	15	Adult
Liver-Spleen Imaging	1	4.76	2.60	1.86	1.61	1.35	1
	2	2.14	1.64	1.31	1.28	1.29	1
$MF \times \frac{1890\ gm}{liver\ wt}$	3	0.80	0.89	0.78	0.93	1.08	1
	4	2.35	1.51	1.49	1.31	1.04	1
Brain Imaging	1	5.96	2.96	2.38	1.74	1.24	1
	2	2.68	1.86	1.67	1.38	1.19	1
$MF \times \frac{70\ kg}{Wt}$	3	1	1	1	1	1	1
	4	2.94	1.72	1.90	1.41	0.96	1
Thyroid Imaging	1	2.13	2.00	1.58	1.38	1.26	1
	2	0.96	1.26	1.11	1.10	1.20	1
$MF \times \left(\frac{20\ gm}{thyroid\ wt}\right)^{2/3}$	3	0.36	0.68	0.66	0.80	1.01	1
	4	1.05	1.16	1.26	1.17	0.97	1

CLINICAL APPLICATION

Static Imaging Studies

The effects of the method of dosage computation on ID for static imaging are given in Table 4. For thyroid (thin organ) imaging, adult ID is best approximated by adjusting dosages by BSA (Method 2), which is very similar to Webster's rule (Method 4). For liver-spleen and brain studies (thick organs), adjustment of dosage by Wt (Method 3) gives the closest approximation of adult ID.

Table 5 describes the relative number of counts needed for pediatric static images to exhibit the same ID as adult images. For equivalent ID, far fewer counts are needed for small patients. If it is customary to obtain 1 million counts for the anterior view of the liver for an adult, an image of similar ID in a newborn will contain only 154,000 counts.

The effects of the method of dosage computation on radiation absorbed dose are given in Table 6 for selected target organs, and Table 7 for the whole body. These tables list the adult dosage of [^{99m}Tc]DTPA as 5 mCi for a dynamic renal study: hence, radiation absorbed doses must be multiplied by four for brain imaging with an adult dosage of 20 mCi. In general, adjustment of dosages by Wt yields radiation absorbed doses that are less than those for an adult, and adjustment by BSA or Webster's rule gives doses that are slightly greater than those for an adult. These differences are most pronounced for younger patients.

Dynamic Imaging Studies

The effects of the method of dosage computation on the quality of dynamic imaging studies are given in Table 8. For dynamic renal imaging, where the quality of the study is determined by the statistical reliability of each point on the renogram, adjustment of dosage by Ht (Method 1) yields renograms of similar quality in all age groups. Adjustment by BSA or Wt, the two most commonly used methods, will yield renograms with far fewer counts in small patients.

If study quality for gated cardiac ventriculography were adequately assessed by ID, Table 8 indicates that studies of adult quality would be obtained by adjusting dosages by BSA or Webster's rule. However, if total ventricular counts were the important consideration in study quality, then dosages larger than those prescribed by any of these methods would be needed, as even adjustment by Ht does not yield as many counts for children as for adults.

TABLE 5
Relative Counts Needed for Equivalent Information Density

Study	Newborn	Age (yr) 1	5	10	15	Adult
Liver-spleen imaging	0.1546	0.3018	0.4834	0.6260	0.7887	1
Brain imaging	0.4036	0.7828	0.8713	0.9554	0.9610	1
Thyroid imaging	0.1357	0.2154	0.3969	0.5787	0.7504	1

TABLE 6
Radiation Absorbed Dose: Target Organ
(mrad)

Item	Method	Newborn	Age (yr) 1	5	10	15	Adult
Liver-spleen imaging	1	4,200	2,802	2,882	2,237	1,885	1,700
[^{99m}Tc]sulfur colloid	2	1,886	1,766	2,021	1,780	1,803	1,700
Adult dosage = 5 mCi	3	704	947	1,209	1,288	1,514	1,700
Target = liver	4	2,071	1,625	2,300	1,812	1,455	1,700
Dynamic renal study	1	640	323	313	172	240	200
[^{99m}Tc]DTPA	2	254	204	220	216	236	200
Adult dosage = 5 mCi	3	95	109	132	156	180	200
Target = kidney	4	278	188	250	220	186	200
(Note: Multiply all values by 4 for brain imaging)							
Thyroid imaging	1	13,900	14,220	9,580	7,190	5,940	3,900
[^{123}I]NaI	2	6,240	8,970	6,720	5,720	5,680	3,900
Adult dosage = 300 μCi	3	2,330	4,810	4,020	4,140	4,770	3,900
Target = thyroid	4	6,880	8,250	7,650	5,820	4,580	3,900
Thyroid uptake	1	23,170	23,710	16,290	11,980	10,370	6,500
[^{131}I]NaI	2	10,400	14,942	11,420	9,540	9,920	6,500
Adult dosage = 5 μCi	3	3,890	8,010	6,830	6,900	8,330	6,500
Target = thyroid	4	11,430	13,750	13,000	9,710	8,000	6,500

Nonimaging Study: Thyroid Uptake

Table 9 demonstrates how much longer the examination times are for children than adults. Even if dosages are scaled by Ht, the study will take 3.5 times longer for a newborn than an adult and the radiation dose to the thyroid will be 23 rad compared with 6.5 rad for an adult. If dosages are adjusted by Wt, the radiation dose to the thyroid will only be 3.9 rad, but the examination

TABLE 7
Radiation Absorbed Dose: Whole Body
(mrad)

Item	Method	Newborn	Age (yr) 1	5	10	15	Adult
Liver-spleen imaging	1	203	121	119	108	94	95
[^{99m}Tc]sulfur colloid	2	91	76	50	72	76	95
Adult dosage = 5 mCi	3	34	41	83	86	90	95
	4	100	70	95	87	73	95
Dynamic renal study	1	246	134	135	116	99	80
[^{99m}Tc]DTPA	2	110	84	94	92	95	80
Adult dosage = 5 mCi	3	41	45	56	68	80	80
	4	122	78	108	94	76	80
(Note: Multiply all values by 4 for brain imaging)							
Gated cardiac study	1	1,488	754	626	599	471	500
[^{99m}Tc]red cells	2	650	475	439	477	451	500
Adult dosage = 25 mCi	3	243	255	263	345	379	500
	4	714	437	500	485	364	500
Thyroid imaging	1	30	17	15	12	13	9
[^{123}I]NaI	2	14	11	10	10	12	9
Adult dosage = 300 μCi	3	5	6	6	7	10	9
	4	15	10	12	10	10	9

TABLE 8
Dynamic Imaging Studies
Relative Quality

Study and factor determining quality	Method	Newborn	Age (yr) 1	5	10	15	Adult
Dynamic renal counts	1	0.776	0.804	1.047	1.104	1.123	1
	2	0.348	0.507	0.734	0.879	1.074	1
$MF \times \frac{70\ kg}{Wt} \times \frac{BSA}{1.73\ m^2}$	3	0.130	0.272	0.439	0.636	0.902	1
	4	0.383	0.466	0.836	0.894	0.866	1
Gated cardiac study information density	1	2.570	1.572	1.595	1.408	1.147	1
	2	1.154	0.991	1.120	1.121	1.098	1
$MF \times \frac{70\ kg}{Wt} \times \left(\frac{heart\ wt}{300\ g}\right)^{1/3}$	3	0.431	0.531	0.670	0.811	0.922	1
	4	1.268	0.912	1.273	1.141	0.885	1
Gated cardiac study counts	1	0.477	0.444	0.715	0.926	0.975	1
	2	0.214	0.280	0.844	0.737	0.933	1
$MF \times \frac{70\ kg}{Wt} \times \frac{heart\ wt}{300\ g}$	3	0.080	0.145	0.300	0.533	0.783	1
	4	0.235	0.257	0.571	0.751	0.752	1

will take 20 times longer than that needed for an adult in order to obtain equivalent counting statistics. This relationship between the thyroid radiation absorbed dose and the time needed to perform the uptake depends on the size of the thyroid and is not significantly influenced by thyroid uptake. If a patient's uptake were twice as high, half the dosage could be used and the whole body dose would be slightly less, but the activity in the thyroid and the thyroid radiation absorbed dose would still be the same.

DISCUSSION

The selection of radiopharmaceutical dosages in children is complicated by several conflicting interests. The analysis presented here assumes that the spatial resolution requirements for static imaging are the same in children as adults. However, it could also be argued that the absolute sizes of many abnormalities are smaller in children than in adults, and that greater spatial resolution is required for pediatric studies. This requirement would force the use of high resolution collimators that are less efficient than those usually used for adults. High spatial resolution also demands minimal patient movement, a problem with small children that can be addressed in part by reducing imaging time. These factors suggest that relatively large dosages should be used for pediatric nuclear medicine examinations. However, it is desirable to limit radiation exposure, particularly in children. Developing tissues (e.g., the brain during the first year of life), are thought to be more radiosensitive than are tissues that have completed growth and differentiation (*14*). Children also have a longer life expectancy over which the adverse effects of irradiation may be manifested. The selection of radiopharmaceutical dosages must balance these considerations. To do so, it is necessary to identify the factors that contribute most to the diagnostic adequacy of a study.

Static Imaging Studies

Webster (*3*) suggested that ID is the most important consideration for static imaging, and that equivalent ID is achieved if dosages are adjusted by organ area, esti-

TABLE 9
Relative Time Needed for Thyroid Uptake

Method	Newborn	Age (yr) 1	5	10	15	Adult
1	3.452	2.320	1.596	1.252	1.061	1
2	7.686	3.681	2.276	1.573	1.109	1
3	20.576	6.863	3.804	2.174	1.231	1
4	6.998	4.000	2.000	1.545	1.376	1

mated as (organ weight/adult organ weight)$^{2/3}$. He also demonstrated that organ area is closely approximated by (age in years + 1)/(age in years + 7) (*3*). However, the difference between dosage adjustment by organ area and by BSA is not great, and BSA was selected for comparison to the other methods because it is more commonly used. Table 3 demonstrates that Webster's rule closely correlates with BSA; hence these methods can be used interchangeably, so long as the patient is of appropriate size for age.

The formulation for static imaging of children presented here suggests that an ID approximately that for an adult is obtained over the same imaging time if dosages are adjusted by BSA for "thin" organs, and by Wt for "thick" organs. Because dosages calculated by Wt often seem too low for very young patients, it has been suggested that there is a minimum required dosage regardless of how small the patient is. Typical minimum dosages include: [^{99m}Tc]pertechnetate for brain imaging-2 mCi, [^{99m}Tc]diphosphonate for bone imaging-2 mCi, and [^{99m}Tc]sulfur colloid for liver-spleen imaging-0.75 mCi (*15*). However, the "need" for such dosages may arise from a desire for a certain number of total counts on each image rather than a specified ID; images of equal ID will contain far fewer counts in small patients. The theoretical adequacy of very small dosages in very small children can be supported by analogy to imaging small organs, such as the thyroid in adults. Although high resolution is required for this study, the thyroid typically has only 20 μCi of ^{123}I at the time of imaging (dosage = 300 μCi, 6-hr uptake = 10%, 6-hr decay correction = 0.73), which is far less than the suggested minimum dosage for liver-spleen imaging in infants.

When radiopharmaceutical dosages are adjusted by BSA, radiation absorbed doses are slightly greater than those for adults. Adjustment of dosages by Wt yields radiation doses that are less than those for adults, with savings of up to 50% in the smallest patients. The radiation dose data suggest that adjustment by Wt should be recommended for all static imaging procedures, recognizing that longer imaging times will be required for "thin" organs to obtain adult ID. These data are also important to consider in keeping the radiation absorbed doses for pediatric nuclear medicine examinations competitive with those delivered by other imaging modalities. Even with the Wt method, the dose reduction in small children is less pronounced than the reduction in x-ray exposure attributable to reduced attenuation of the beam used to radiograph small children.

The static imaging studies examined in this report were selected because the distributions of the radiopharmaceutical in both the body and target organ are well defined. For other static imaging studies these distributions are not as easily described, and similar analysis must be regarded as more speculative. For bone imaging, the tracer is distributed throughout extracellular fluid, so that adjustment of dosages by Wt should yield similar peak blood concentrations in patients of all ages. With similar blood concentrations, uptake per gram of cortical bone is likely to be roughly equivalent, although this may vary with age. Since the entire thickness of the bone is imaged, the analysis presented for "thin" organs is likely to be applicable for bone imaging, and dosages could be adjusted by either BSA or Wt. Although adjustment by Wt would require slightly longer imaging times, it is likely that with this method the whole body doses would be less for children than adults. However, the major difference between adult and pediatric dosimetry for bone imaging is the focally higher doses at the growth plates which is due to their physiologically accentuated uptake of the tracer (*16*). Similar considerations also apply to the radiation dosimetry for gallium-67 citrate imaging (*17*). The dosage requirements for hepatobiliary studies are extremely complex and depend on hepatic function, biliary anatomy, and the clinical question that the study is intended to answer. For studies performed to exclude acute cholecystitis in patients with normal hepatic function, the tracer is highly concentrated in the biliary system and the presence or absence of cystic duct obstruction is readily identifiable. The images from these studies often demonstrate such high concentrations of activity in the biliary system that the photographic intensity must be turned down, suggesting that smaller dosages may suffice. However, the situation is less favorable in studies performed to evaluate potential biliary atresia in neonates. In these patients, hepatic function is poor and blood concentration (image background) remains high. Even if excretion does take place, the concentration of the tracer is low and thus the target to background ratio is very poor. These complexities suggest that no simple dosage schedule can be recommended for hepatobiliary studies and that it is likely that dosages may need to be varied several fold between patients depending on physiologic and anatomic considerations.

Dynamic Imaging Studies

The data presented above suggest that a different approach to calculating radiopharmaceutical dosages is needed for children undergoing dynamic imaging procedures. For dynamic renal imaging, renograms of quality similar to adult studies require adjustment of dosages by Ht. Since renal function is analyzed during the accumulation phase of the renogram, lower radiopharmaceutical dosages cannot be compensated for by using longer imaging times. Although the analysis presented here does not account for reduced tissue attenuation of radiation in small children, this influence on the required dosage is offset by a lower GFR during the

first year of life, even when expressed per BSA. Adjusting the radiopharmaceutical dosage to provide an adequate statistical quality of the renogram also has important implications for patients with significant impairment of renal function. Larger dosages will be required in these patients, even though their radiation absorbed doses are also increased because of slow biological clearance.

A major consideration in dosage selection for dynamic renal studies is the method of renogram analysis. If the initial passage of the bolus through the kidney and aorta is analyzed, the frame time must be short (one second) and a relatively large radiopharmaceutical dosage (^{99m}Tc 15 mCi) is needed (*18,19*). If a "flow study" is not included, less activity is needed for analysis of both relative and combined renal function from the accumulation phase of the renogram. The two major methods of determining the rate of tracer accumulation in the kidney are measurement of the slope of the renogram during the accumulation phase (*20,21*) and measurement of total counts over a fixed time interval (*22,23*). Previous work has indicated that the slope method estimates renal function more accurately than the total counts (area) method (*24*). However, the slope method requires higher dosages since each point on the renogram needs to be defined with greater statistical precision. The suggestion that radiopharmaceutical dosages for dynamic renal studies should be adjusted by Ht, rather than Wt or BSA, does not necessarily imply that the dosages currently used for children need to be increased. Rather, it may be feasible to decrease the dosages used for adults. The examination of radiation dosimetry described here is based on an adult dosage of 5 mCi of [^{99m}Tc]DTPA, which is substantially less than that used in many laboratories. Even dosages not exceeding 2 mCi usually provide adequate renograms in adults, if a radionuclide angiogram is not included.

For gated cardiac ventriculography, adjustment of doses by BSA would be sufficient if study quality were adequately expressed by ID. However, the need for better resolution of ventricular edges (to obtain equivalent relative resolution) suggests that the total number of cardiac counts should be as high in children as in adults. The similarity of recommendations for counts per frame needed for adults (200,000 (*25*) or 300,000 (*26*)) and children (250,000 (*27*) or 350,000 (*28*)) corroborates the contention that study quality is determined by total ventricular counts rather than ID. Equal count rates require dosages even larger than those computed by Ht, which would lead to undesirably high radiation absorbed doses in children. Fortunately, it is possible to compensate for a lower count rate by prolonging the duration of imaging or by using fewer frames per cardiac cycle to obtain the desired number of counts per frame. Heavy temporal smoothing has the same effect as using fewer frames per cycle; both procedures increase the effective number of counts per frame at the expense of temporal resolution. This trade-off may be an acceptable compromise for children. Measurement of the ventricular filling rate has been shown to supplement the information provided by the ejection fraction for the identification of coronary artery disease in adults (*29,30*), and this measurement requires higher temporal resolution than that needed for the ejection fraction (*31*). This index of diastolic function may also help define myocardial pathophysiology in children; however, this possibility has not yet been demonstrated clinically.

Since lower cardiac count rates can be compensated for either by prolonging imaging or by using fewer frames, there is some flexibility in radiopharmaceutical dosage selection. Recognizing that even adjustment by Ht yields lower count rates in children compared to adults, we recommend dosages no smaller than those determined by BSA, with serious consideration to adjustment by Ht. Adjustment by Ht will yield greater radiation doses than those for many nuclear medicine procedures, with whole body doses of 1,450 mrad for a newborn and 750 mrad for a one year old child. However, this recommendation may permit more accurate edge determination and thereby improve the estimation of the ejection fraction. With dosages calculated by BSA, we have found that examinations in young children often take 20 to 30 min per view, even in the presence of significant cardiomegaly which increases the total ventricular count rate. Similarly lengthy examination times have also been reported by others (*28,32*). Adjustment by Wt necessitates even greater prolongation of the study. Prolongation is not only clinically inconvenient; it also increases the likelihood of patient motion and a consequent reduction in spatial resolution.

For first-pass cardiac ventriculography additional imaging time cannot be used to enhance studies performed in children. Because cardiac structures are separated temporally as well as spatially, spatial resolution is not as critical in these examinations as it is for gated studies. However, obtaining sufficient counts for a valid time-activity curve is very important in first-pass studies. To accomodate high count rates, some investigators believe that first pass studies are best performed with a multicrystal scintillation camera (*30*), although others have reported good results with a single crystal detector (*33*). Since the time-activity curve depends on total counts rather than counts per unit area, it might appear that dosages even larger than those calculated by Ht would be needed, and this could not be compensated for simply by prolonging imaging as can be done with gated studies. Although there is less attenuation of photons in small children, this gain is offset by more rapid transit through the central circulation.

Despite these theoretical hindrances to performing

first-pass studies in children, Kurtz et al. (*34*) have reported excellent results with first-pass determinations of left ventricular ejection fraction in children using 200 μCi/kg of [^{99m}Tc]pertechnetate. This is equivalent to an adult dosage of 14 mCi adjusted by Wt. Two considerations that may explain these results are the use of a Fast Fourier Transform to suppress statistical noise, and the use of a relatively slow frame rate (frame times of 100 msec, or 67 msec in children whose heart rate was > 120 cycles/min). These frame times indicate that the cardiac cycle was divided into approximately eight frames. For comparison, the recommended frame time of 40 msec for adults (*33,35*), yields 20 frames/cycle at a heart rate of 75, and even shorter frame times (25 msec) are recommended if analysis is to include measurement of the ventricular filling rate (*30*). Thus, Kurtz et al. (*34*) obtained sufficient counts per frame in children by using fewer frames per cycle. Although the temporal resolution was less than that usually used for adults, this reduction did not interfere with the calculation of the ejection fraction. Bacharach et al. (*31*) examined the temporal resolution required for measuring various parameters of the ventricular time-activity curve. These investigators found that for exercise studies (heart rate = 140), the ejection fraction could be measured with a frame time of 40 msec, which gives 11 frames/cycle. This degree of temporal resolution is close to that used by Kurtz et al (*34*), and less than that usually employed for adults. Limiting temporal resolution to no greater than that required by the physiologic characteristic being measured will prevent the need for unnecessarily high dosages.

Nonimaging Studies

Thyroid uptake depends on total counts rather than ID. Children would have thyroid count rates similar to adults only if they were given equal dosages, an inadvisable procedure because of the radiation burden. Adjusting dosages by Wt or BSA seems reasonable, even though counting times will be increased susbstantially by this approach. Small amounts of patient motion will not affect the thyroid uptake measurements; hence prolonged counting is merely inconvenient. Mitchell (*3*) has suggested that the radiopharmaceutical dosage needed for a thyroid uptake (or any other organ counting study) can be reduced in children by decreasing the thyroid-detector distance. Although a shorter distance certainly should be used, it is also necessary to use more restrictive collimation in children to distinguish thyroid activity from the surrounding tissue. With more restrictive collimation and a shorter distance, little change in detector sensitivity will be realized. In general, organ counting studies in children are hindered by their reliance on total radioactivity rather than ID, and by the increased difficulty in limiting the field-of-view of the detector to the organ of interest in small patients.

Additional Considerations

Most of this analysis has been directed to the question of how adult dosages should be adjusted for pediatric patients. Further work is needed to answer the more difficult question of how adult dosages are rationally determined. This work must balance the benefits of study quality against the risks of radiation absorbed dose. Because imaging time has financial ramifications, study quality and radiation exposure must also be weighed against patient cost.

Dosage requirements are also influenced by the state of instrumentation development. Increasing ID improves lesion detectability up to a point of diminishing returns because of limitations in detector resolution. Improvements in scintillation camera performance may paradoxically result in increased dosage requirements, as the benefits of a greater ID can be realized.

The development of single photon emission computed tomography (SPECT) has also caused an escalation of radiopharmaceutical dosages. Recent reports with SPECT indicate that dosages of 6 mCi of [^{99m}Tc]sulfur colloid for liver-spleen imaging (*36*) and 25 mCi of [^{99m}Tc]diphosphonate for bone imaging (*37*) are now in common use in leading nuclear medicine laboratories. Improved resolution and the added perspective of tomography undoubtedly have some clinical benefit; however, benefit is not without an added radiation burden and extra patient cost. The analysis presented here indicates that for both gated and first-pass cardiac studies, greater temporal resolution, and therefore a larger radiopharmaceutical dosage and radiation absorbed dose are needed if analysis is to include not only the ejection fraction, but also ventricular filling rates. The pertinent issue is not whether an entire study has favorable risk-benefit and cost-benefit ratios; it is whether a marginal improvement in resolution, the inclusion of tomography, the added information from the ventricular filling rate, the inclusion of a flow study with a dynamic renal study, etc. are worth the extra radiation and extra cost required for the addition. This issue deserves continuing close scrutiny.

Finally, continuing comparison of nuclear medicine studies with other modalities is necessary. Risk-benefit and cost-benefit analysis in nuclear medicine must consider not only the risks, costs, and benefits of a particular examination, but also how these characteristics compare to alternative procedures. Rare earth screens and improved fluoroscopic systems (*38*) have significantly reduced radiation exposure for conventional radiographic studies, and ultrasound and magnetic resonance imaging use no ionizing radiation. All of these factors must be considered in a rational selection of radiopharmaceutical dosages for diagnostic nuclear medicine procedures for both children and adults.

REFERENCES

1. Goetz WA, Hendee WR, Gilday DL: In vivo diagnostic nuclear medicine: pediatric experience. *Clin Nucl Med* 8:434-439, 1983
2. SNM Newsline. *J Nucl Med* 26:555-556, 1985
3. Mitchell TG: Practical factors in dose reduction. In *Pediatric Nuclear Medicine*, James AE, Wagner HN, Cooke RE, eds. Philadelphia, W. B. Saunders, 1974, pp. 22-34
4. Webster EW, Alpert NM, Brownell GL: Radiation doses in pediatric nuclear medicine and diagnostic x-ray procedures. In *Pediatric Nuclear Medicine*, James AE, Wagner HN, Cooke RE, eds. Philadelphia: W. B. Saunders, 1974, pp 34-58
5. *Height and Weight of Children, United States* (Washington, D.C.: Dept. of Health, Education and Welfare, Public Health Service, 1970). as quoted in Lowery GH: *Growth and Development of Children*, 7th ed. Chicago, Year Book Medical Publishers, 1978, pp 84-85
6. Winkelstein JA: *The Harriet Lane Handbook: A Manual for Pediatric House Officers*, Chicago, Year Book Medical Publishers, 1979, p 223
7. *International Commission on Radiologic Protection: Report of Task Force on Reference Man*, ICRP Publication 23, New York, Pergamon Press, 1975
8. Poston J: The effects of body size and organ size on absorbed dose: There is no standard patient. In *Radiopharmaceutical Dosimetry Symposium* HEW Publication (FDA) 76-8044 Bureau of Radiologic Health, Food and Drug Administration, Cloutier RJ, Coffey JL, Snyder WS, et al., eds. Rockville, MD, 1976
9. Lowrey GH: *Growth and Development of Children*, 7th ed. Chicago, Year Book Medical Publishers, 1978, p 454
10. Kereiakes JG, Rosenstein M: *Handbook of Radiation Doses in Nuclear Medicine and Diagnostic X-ray*, Boca Raton, Florida, CRC Press, 1980
11. Kereiakes JG, Feller PA, Ascoli FA, et al: Pediatric radiopharmaceutical dosimetry. In *Radiopharmaceutical Dosimetry Symposium*, HEW Publication (FDA) 76-8044, Bureau of Radiologic Health, Food and Drug Administration, Cloutier RJ, Coffey JL, Snyder WS, et al., eds. Rockville, MD, 1976
12. Roedler HD, Kaul A, Hine GJ: *Internal Radiation Dose in Diagnostic Nuclear Medicine*, Berlin, Verlog H. Hoffman, 1978
13. NCRP Report No. 73: *Protection in Nuclear Medicine and Ultrasound Diagnostic Procedures in Children*, Bethesda, MD, National Council on Radiation Protection and Measurements, 1983
14. National Research Council Committee on the Biological Effects of Ionizing Radiations: *The Effects on Populations of Exposure to Low Levels of Ionizing Radiation: 1980*. Washington, DC, National Academy Press, 1980. pp 477-493
15. Alderson PO, Gilday DL, Wagner HN: *Atlas of Pediatric Nuclear Medicine*, St. Louis, C. V. Mosby, 1978, p 4
16. Thomas SR, Gelfand MJ, Kereiakes JG, et al: Dose to metaphyseal growth complexes in children undergoing ^{99m}Tc-EHDP bone scans. *Radiology* 126:193-195, 1978
17. Thomas SR, Gelfand MJ, Burns GS, et al: Radiation absorbed-dose estimates for the liver, spleen, and metaphyseal growth complexes in children undergoing gallium-67 citrate scanning. *Radiology* 146:817-820, 1983
18. Rosenthall L: Radiotechnetium renography and serial radiohippurate imaging for screening renovascular hypertension. *Semin Nucl Med* 4:97-116, 1974
19. Hilson AJW, Maisey MN, Brown CB, et al: Dynamic renal transplant imaging with Tc-99m DTPA (Sn) supplemented by a transplant perfusion index in the management of renal transplants. *J Nucl Med* 19:994-1000, 1978
20. Piepsz A, Denis R, Ham HR, et al: A simple method for measuring separate glomerular filtration rate using a single injection of ^{99m}Tc-DTPA and the scintillation camera. *J Pediatr* 93:769-774, 1978
21. Tamminen TE, Riihimaki EJ, Tahti EE: A gamma camera method for quantification of split renal function in children followed for vesicoureteral reflux. *Pediat Radiol* 7:78-84, 1978
22. Pieretti R, Gilday D, Jeffs R: Differential kidney scan in pediatric urology. *Urology* 4:665-668, 1974
23. Gates GF: Glomerular filtration rate: Estimation from fractional renal accumulation of ^{99m}Tc-DTPA (stannous). *AJR* 138:565-570, 1982
24. Shore RM, Koff SA, Mentser M, et al: Glomerular filtration rate in children: determination from the Tc-99m-DTPA renogram. *Radiology* 151:627-633, 1984
25. Berman DS, Maddahi J, Garcia EV, et al: Assessment of left and right ventricular function with multiple gated equilibrium cardiac blood pool scintigraphy. In *Clinical Nuclear Cardiology*, Berman DS, Mason DT, eds. New York, Grune and Stratton, 1981, p 224-284
26. Strauss WH, Pitt B: Gated blood pool imaging. In *Cardiovascular Nuclear Medicine*, Strauss WH, Pitt B, eds. 2nd ed., St. Louis, C. V. Mosby, 1979, p. 126-147
27. Hurwitz RA, Treves S, Freed M, et al: Quantification of aortic and mitral regurgitation in the pediatric population: evaluation by radionuclide angiocardiography. *Am J Cardiol* 51:252-255, 1983
28. Sty JR, Starshak RJ, Miller JH: *Pediatric Nuclear Medicine*, Norwalk, CT, 1983, pp 27-52
29. Bonow RO, Bacharach SL, Green MV, et al: Impaired left ventricular diastolic filling in patients with coronary artery disease: Assessment with radionuclide angiography. *Circulation* 62:315-323, 1981
30. Polak JF, Kemper AJ, Bianco JA, et al: Resting early peak diastolic filling: a sensitive index of myocardial dysfunction in patients with coronary artery disease. *J Nucl Med* 23:471-478, 1982
31. Bacharach SH, Green MV, Borer JS, et al: Left ventricular peak ejection rate, filling rate, and ejection fraction: frame rate requirements at rest and exercise. *J Nucl Med* 20:189-193, 1979
32. Treves S, Royal H, Babchyck B: Pediatric nuclear cardiology. In *Pediatric Cardiovascular Disease* (*Cardiovascular Clinics* 11/2). Engle MA, ed. Philadelphia, F. A. Davis, 1981, pp 247-274
33. Jengo JA, Mena I, Blaufuss A, Criley JM: Evaluation of left ventricular function (ejection fraction and segmental wall motion) by single pass radioisotope angiography. *Cardiology* 57:326-332, 1978
34. Kurtz D, Ahnburg DS, Freed M, et al: Quantitative radionuclide angiocardiography: determination of left ventricular ejection fraction in children. *Br Heart J* 38:966-973, 1976
35. Gordon DG, Ashburn WL, Slutsky RA: Assessment of ventricular function by first-pass radionuclide angiography. In *Clinical Nuclear Cardiology*, Berman DS, Mason DT, eds. New York, Grune and Stratton, 1981, pp 204-223

36. Keyes JW Jr, Singer D, Satterlee W, et al: Liver-spleen studies with the rotating gamma camera II: Utility of tomography. *Radiology* 153:537-541, 1984
37. Collier BD, Johnson RP, Carrera GF, et al: Painful spondylolysis or spondylolisthesis studied by radiography and single photon emission computed tomography. *Radiology* 154:207-211, 1985
38. Wesenberg RL, Amundson GM: Fluoroscopy in children: Low-exposure technology. *Radiology* 153:243-247, 1984