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EDITORIAL

Can DMSA Detect Early Renal Injury in Children with Vesicoureteral Reflux?

Vesicoureteral reflux occurs in approximately 1%–2% of the pediatric population. These children are at increased risk for renal scarring, hypertension and, in some instances, progression to chronic renal failure if left untreated (*1*). Extremely poor growth of scarred kidneys has been noted in children greater than 5 yr of age (*2*), however, little is known about the effects of persistent vesicoureteral reflux in patients with undamaged kidneys (*3*).

The recently published proceedings of the International Workshop on Reflux and Pyelonephritis (*4*) document the ongoing and progressive nature of renal injury in children with vesicoureteral reflux. Smellie et al. (*5*) originally confined the risk of renal injury to children under 2 yr of age and disclosed by longitudinal studies the continued risk of covert renal scars over subsequent years and potential deleterious outcomes such as hypertension. The association between acute pyelonephritic episodes and eventual scarring has been relatively well defined in both experimental animals and clinical studies, but we may speculate that there are more subtle methods of renal injury which may account for the eventual development of renal scars (*6*). By the time scarring has occurred, no remedial or preventive measures can be taken, thus a sensitive test which could show evidence of renal injury early in the process of the pathogenesis would clearly be a great advance.

Gamma camera methods of renal function measurement have gained popularity because of their relative speed, simplicity and ability to estimate split renal function without the need for ureteral catheterization. These factors are particularly important in the pediatric population in whom studies which are noninvasive and associated with minimal risk and discomfort are advantageous such as in the assessment of urinary tract infection (*7*). Radionuclide scintigraphy has proven to be a sensitive indicator of reflux (*8*), while cortical agents such as technetium-labeled glucoheptonate and dimercaptosuccinic acid (^{99m}Tc-DMSA) are useful in evaluating split renal function, to distinguish between acute pyelonephritis and cystitis, and to assess changes in function and the development of scarring over time (*9*). Although glucoheptonate has the advantage of a lower radiation dose, retention in the renal pelvis can interfere with interpretation and cause artifacts when using SPECT imaging techniques. Because of the excellent cortical visualization obtained with ^{99m}Tc-DMSA, of which 40% is bound in the tubules, it has become the agent of choice for SPECT imaging and for quantitation of renal function. SPECT imaging obviates the need for depth correction and minimizes the effects of background activity that have limited the usefulness of planar scintigraphy in measuring renal function. Groshar et al. (*10*) have previously validated a method of separating normal from diseased kidneys using absolute individual kidney uptake of ^{99m}Tc-DMSA.

In this issue, Groshar et al. have provided data to support the use of ^{99m}Tc-DMSA quantitative SPECT studies as determinants of individualized kidney unit function in children with vesicoureteral reflux. In normal controls, they found a significant correlation between age and functional kidney volume as measured by ^{99m}Tc-DMSA renal uptake. Because of the inverse correlation between age and renal uptake of ^{99m}Tc-DMSA both globally and per unit volume, it is important that controls and subjects are age matched. Although kidneys associated with significant reflux had reduced functional volume, it is interesting that the percent ^{99m}Tc-DMSA uptake per unit volume was similar to that measured in controls. Contralateral normal kidneys in these subjects had significantly increased global uptake secondary to increased ^{99m}Tc-DMSA uptake per unit renal volume, which may represent compensatory hyperfunctioning.

The techniques described in this paper may well fulfill the need for more sensitive and specific indicators of early renal injury, and we would suggest that others explore this same methodology in future trials to confirm or validate these findings. These techniques could also be explored as a means of assessing early renal injury in populations other than those with reflux, such as infants with antenatally detected hydronephrosis. Some of these infants have had similarly detected global reduction in renal volume associated with vesicoureteral reflux (*11*). It may be that the techniques

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applied herein can also be applied to infants and young children with risks other than vesicoureteral reflux, such as obstruction.

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Condensed from *15 Years Ago*

Cellular Radiation Doses of Labeled Neutrophils and Platelets

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Radiation doses were calculated for human neutrophils and platelets labeled by phosphorus-32, chromium-51, gallium-67, technetium-99m, indium-111 and mercury-197. The cells were assumed to be spheres with radii of 4.87 μm and 1.07 μm, respectively, with all the radioactivity at either the center or uniformly distributed on the surface. Surprisingly high dose rates were found, due primarily to the small mass and therefore high radioactive concentration and to low-energy electrons, such as Auger electrons. Average total doses to these cells during their effective lifetime in the blood are presented.

Internal Doses and Rates for Six Different Radionuclides Used in Cell Labeling

Cells	Nuclide	Dose Rate for 100 mCi/g (rads/hr)	Dose Rate for 1 mCi in cells from 30 ml blood (rads/hr)	Effective $t_{1/2}$ in blood (hr)	Dose while circulating (rads)
Neutrophils	P-32	170	24	5.9	200
(r = 4.87 μm)	Cr-51	800	115	5.95	990
	Ga-67	1700	245	5.57	1970
	Tc-99m	630	91	3	390
	In-111	1300	187	5.5	1480
	Hg-197	3500	503	5.5	3990
Platelets	P-32	35	8.4	82	1000
(r = 1.07 μm)	Cr-51	800	193	93	25900
	Ga-67	1300	313	45	20320
	Tc-99m	520	125	5.7	1030
	In-111	885	213	42	12900
	Hg-197	2800	675	41	39940

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