4. Tobes MC, Jaques S, Wieland DM, et al. Effect of uptake-one inhibitors on the uptake of norepinephrine and metaiodobenzylguanidine. *J Nucl Med* 1985;26:897–907.
5. Nakajyo M, Shimabukuro K, Yosimura, et al. Iodine-131-metaiodobenzylguanidine intra- and extra-vesicular accumulation in the rat heart. *J Nucl Med* 1986;27:84–89.
6. Jaques S, Tobes MC. Comparison of the secretory mechanisms of metaiodobenzylguanidine and norepinephrine from cultured bovine adrenomedullary cells [Abstract]. *J Nucl Med* 1985;25(suppl):17.
7. Fagret D, Eric-Wolf J, Vanzetto G, Borrel E. Myocardial uptake of metaiodobenzylguanidine in patients with left ventricular hypertrophy secondary to valvular aortic stenosis. *J Nucl Med* 1993;34:57–60.
8. Rabinovitch MA, Rose CP, Schwab AJ, et al. A method of dynamic analysis of iodine-123-metaiodobenzylguanidine scintigrams in cardiac mechanical overload hypertrophy and failure. *J Nucl Med* 1993;34:589–600.
9. Merlet P, Valette H, Dubois-Rande, et al. Prognostic value of cardiac metaiodobenzylguanidine imaging in patients with heart failure. *J Nucl Med* 1992;33:471–477.
10. Stanton M, Tuli M, Radtke N, et al. Regional sympathetic denervation after myocardial infarction in humans detected noninvasively using ^{123}I-MIBG. *J Am Coll Cardiol* 1989;14:1519–1526.
11. Abe N, Kashiwagi A, Shigeta Y. Usefulness of ^{125}I-metaiodobenzylguanidine uptake for evaluation of cardiac sympathetic nerve abnormalities in diabetic rats. *J Jpn Diab Soc* 1992;35:113–120.
12. Mantysaari M, Kuikka J, Mustonen J, et al. Noninvasive detection of cardiac sympathetic nervous dysfunction in diabetic patients using ^{123}I-metaiodobenzylguanidine. *Diabetes* 1992;41:1069–1075.
13. Cohen HA, Baird MG, Rouleau JR, et al. Thallium-201 myocardial imaging in patients with pulmonary hypertension. *Circulation* 1976;54:790–795.
14. Ohsuzu F, Handa S, Kondo M, et al. Thallium-201 myocardial imaging to evaluate right ventricular overloading. *Circulation* 1980;61:620–625.
15. Weitzenblum E, Moyses B, Dickele MC, Methlin G. Detection of right ventricular pressure overloading by thallium-201 myocardial scintigraphy. *Chest* 1984;85:164–169.
16. Merlet P, Delforge J, Syrota A, et al. PET with ^{11}C-CGP-12177 to assess beta-adrenergic receptor concentration in idiopathic dilated cardiomyopathy. *Circulation* 1993;87:1169–1178.
17. Delforge J, Syrota A, Lancon TP, et al. Cardiac beta-adrenergic receptor density measured in vivo using PET ^{11}C-CGP-12177 and a new graphical method. *J Nucl Med* 1991;32:739–748.
18. Raum WJ, Laks MM, Garner D, Swerdloff RS. Beta-adrenergic receptor and cyclic AMP alterations in the canine ventricular septum during long-term norepinephrine infusion: implications for hypertrophic cardiomyopathy. *Circulation* 1983;68:693–699.
19. Fowler MB, Laser JA, Hopkins GL, Minobe W, Bristow MR. Assessment of the beta-adrenergic receptor pathway in the intact failing human heart: progressive receptor down regulation and subsensitivity to agonist response. *Circulation* 1986;74:1290–1302.
20. Yoshie H, Tobise K, Onodera S. Intraventricular changes in the beta-adrenoceptor adenylate cyclase system of monocrotaline induced right ventricular hypertrophy. *Jpn Circ J* 1994;58:855–865.

Renal Technetium-99m-DMSA SPECT in Normal Volunteers

C. De Sadeleer, A. Bossuyt, E. Goes and A. Piepsz

Departments of Nuclear Medicine, Radiology and Pediatrics, AZ-VUB, Brussels, Belgium

Dimercaptosuccinic acid (DMSA) renal scintigraphy today is considered a sensitive and useful technique for the detection of cortical abnormalities. Recent studies have suggested that lesion detection can be improved by SPECT imaging. This study investigated normal kidneys using different SPECT modalities. **Methods:** Ten young, healthy volunteers with normal clinical history and normal renal ultrasound underwent planar and SPECT DMSA imaging 2 to 4 hr after intravenous injection of ^{99m}Tc-DMSA (185 MBq). Analysis of SPECT data was focused on the homogeneity of cortical uptake (comparison of upper and lower pole activity) as well as on the presence or absence of focal cortical defects. **Results:** No abnormality could be observed on the planar images. SPECT revealed, in seven kidneys (five left and two right), the presence of a hypoactive upper pole. This was visually observed on the coronal slices with up to 35% difference between upper and lower pole. Moreover, three focal cortical defects were visualized on the coronal slices as well as on three-dimensional surface shade displays. **Conclusion:** These normal patterns should be recognized when evaluating a patient with possible renal involvement.

Key Words: renal imaging; technetium-99m-DMSA; SPECT

J Nucl Med 1996; 37:1346–1349

The ^{99m}Tc-dimercaptosuccinic acid (DMSA) renal scan is now widely recognized as a reference method for the evaluation of renal parenchymal disease. The traditional planar technique provides adequate two-dimensional imaging of the renal cortex and most of the validation studies that have defined the clinical value of DMSA scintigraphy were obtained by these conventional planar imaging techniques.

The introduction of high-resolution SPECT offers the opportunity to image the kidneys with even more precise cortical detail. State-of-the-art SPECT not only has a spatial resolution of less than 1 cm, but image contrast is also dramatically improved in the tomographic slices.

Recent reports suggest a higher sensitivity of SPECT compared to planar imaging. However, because of normal variations in kidney anatomy, any increase in contrast obtained by SPECT imaging also creates opportunities for false-positive interpretation.

To evaluate the potential importance of that problem, and to obtain a dataset of normal SPECT images, we compared the results of conventional planar DMSA scintigraphy with those of SPECT using standard and reoriented coronal, sagittal and transverse slices, as well as three-dimensional total organ surface shade images, in a group of normal healthy volunteers.

MATERIAL AND METHODS

Ten healthy volunteers (5 men, 5 women; mean age 23 yr; range 19.7–25.8 yr) were enrolled in this study. They had no history of previous urinary tract disease, fever of unknown origin, hypertension or abdominal trauma. Physical examination, including blood pressure, was normal. Before entering in the study all volunteers underwent an ultrasonographic study of the kidneys in order to exclude any pelvic and calyx distention, renal surface abnormality, expansive masses, tissue texture change or abnormal renal size.

Both planar and SPECT studies were acquired 2 to 4 hr after intravenous injection of 5 mCi (185 MBq) ^{99m}Tc-DMSA. The order of imaging was random.

Planar Imaging

Planar images were obtained with a standard gamma camera equipped with a high-resolution, low-energy collimator, from posteriorly, with the patient in the supine position, and from both posterior oblique sides. Data were acquired in a 256 × 256 matrix, word mode, 300,000 counts per view. No zoom or pinhole images were performed.

Received July 21, 1995; revision accepted Oct. 20, 1995.

For correspondence or reprints contact: Carlos De Sadeleer, MD, A.Z. V.U.B., Department of Nuclear Medicine, Laarbeeklaan 101, 1090 Brussels, Belgium.

SPECT Imaging

SPECT images were obtained with a high-resolution three-headed rotating SPECT camera equipped with a high-resolution, parallel-hole collimator. The gamma camera was rotated clockwise, in a body contour orbit, with a step-and-shoot mechanism, for 30 sec per image and 3 × 48 images per 360°. A matrix of 128 × 128 was used, which equates to approximately 3.6-mm tomographic slices; no zoom was employed. The data were reconstructed by filtered backprojection using a Butterworth filter with a cutoff of 0.55 and an order of 7. No attenuation correction was made.

Three types of display were successively analyzed: the transverse, sagittal and coronal planes; the three same planes after three reorientations around the center of gravity of each separate kidney; the three-dimensional surface shade images of each separate kidney. This last display was part of the computer software, and based on the method described by Höhne and Bernstein (*1*), we produced 24 images per 360°, using a threshold of 40% of the maximum pixel and a linear gray level scale.

In each patient, the images were examined for the detection of hypoactive poles or focal cortical defects. This study was approved by the local medical ethical committee and all volunteers gave written informed consent.

RESULTS

No abnormality was observed on planar images of the 20 examined kidneys. Criteria of normality included normal kidney outlines, good contrast between outer cortical part and inner medullar part, absence of focal cortical defects or polar hypoactivity and a relative left and right DMSA percentage-uptake within the normal range (≥45% relative contribution for each kidney).

Several abnormalities were observed on the SPECT images. A clear interruption of the normal cortical contour was observed in only one kidney. This solitary lesion, lying between two prominent columns of Bertin, was located on the postero-superior side of the left kidney and could be best identified on the coronal slices without reorientation (on four consecutive slices), but also on the three reoriented images and even on the three-dimensional surface shade display (Fig. 1).

In two other kidneys, equivocal cortical defects were seen on the slices. In one of these, a linear area of absent tracer uptake extending from the renal hilum into the parenchyma and with an interruption of the rim of renal cortical uptake was best seen on the reoriented sagittal display and on the three-dimensional surface shade display on the lateral side of the left kidney (Fig. 2).

Hypoactive upper poles were observed in 7 of the 20 kidneys (5 left kidneys and 2 right kidneys) on the coronal slices before as well as after reorientation (Fig. 3). Small regions of interest were drawn over the outer cortex of both renal poles on two central reoriented sagittal and coronal slices. Quantitative evaluation of the maximal upper and lower pole activity revealed differences between the two poles as high as 35%. These hypoactive upper poles were also clearly seen on the three-dimensional surface shade images.

In the other 13 kidneys, the ratio of the maximal upper cortical activity to the maximal lower cortical activity varied from 1.02 to 0.83. The mean upper to lower pole ratio was clearly lower for the left kidney than for the right kidney, 0.79 (SD:0.11) and 0.87 (SD:0.11), respectively (Fig. 4).

DISCUSSION

Renal cortical scintigraphy with ^{99m}Tc-DMSA is an excellent tool for the evaluation of renal cortical defects. It has been shown to be more sensitive than intravenous urography and ultrasonography in the detection of acute pyelonephritis and renal scarring. SPECT improves the detection rate of lesions, in organs like heart and brain, where tracer distribution is fairly homogeneous. This is due to the increased contrast resolution offered by SPECT, which permits better delineation of lesions.

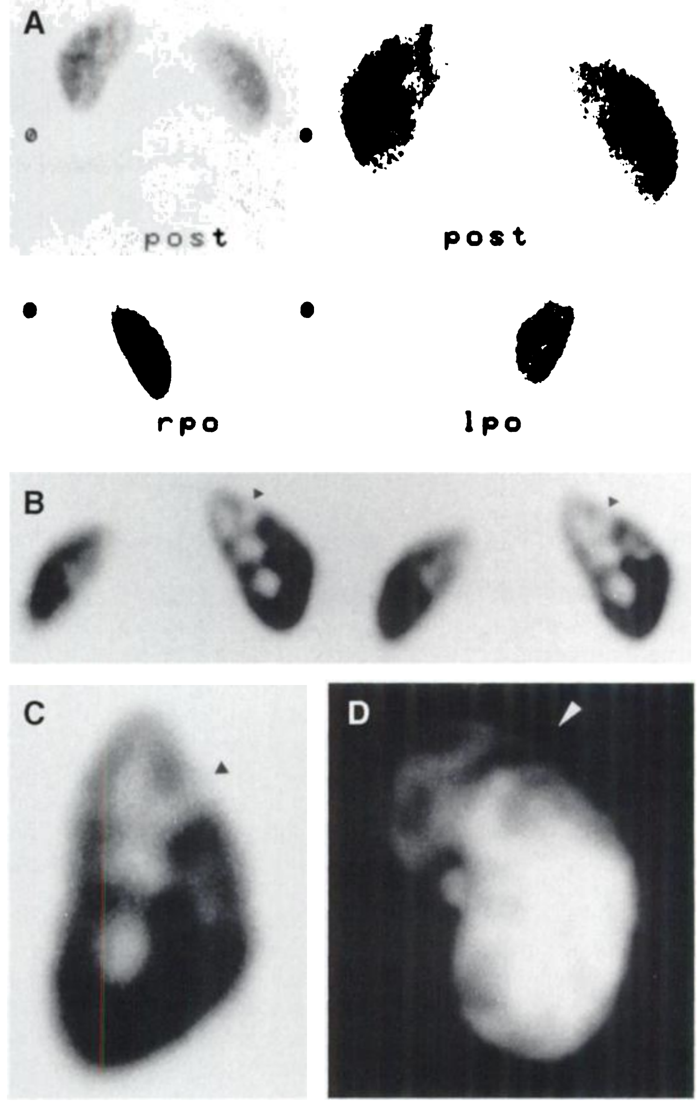

FIGURE 1. (A) Normal planar views (posterior, posterior with magnification, right posterior oblique, left posterior oblique). (B) Two consecutive not reoriented coronal slices, the left kidney is on the right side of the image. (C) Reoriented coronal tomographic section; and (D) three-dimensional display. A definite focal defect is demonstrated on the postero-superior side of the left kidney on the different displays of the SPECT study.

Several patient studies were devoted to the detection of renal cortical defects by means of SPECT. Two studies (*2–4*) using single-headed and triple-headed SPECT, respectively, revealed a higher detection rate of kidney lesions than with conventional planar or pinhole collimator techniques. In one study performed in children (*5*), additional lesions were found with three-headed SPECT in 13 of the 99 examined kidneys. Recent studies seem to confirm the higher detection rate of lesions by means of SPECT, performed either with a single-headed detector (*6,7*) or with a triple-headed detector (*8,9*).

It became evident, however, that the oblique orientation of the kidney could affect visual interpretation of DMSA-SPECT. Rehm et al. (*10*) investigated the influence of orthogonal reorientation (RSPECT); 2% of the regions normal on SPECT changed to abnormal on RSPECT, 22% of the regions abnormal

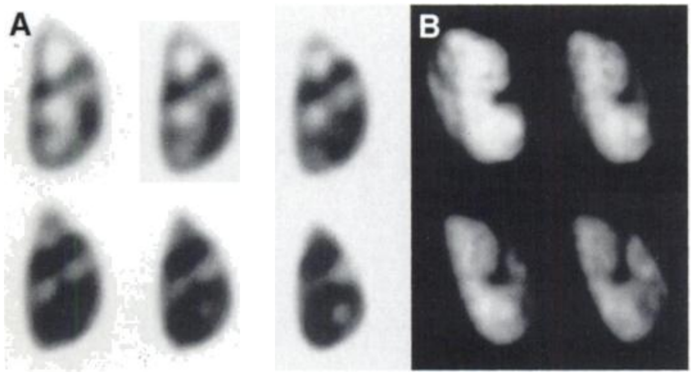

FIGURE 2. (A) Six consecutive reoriented sagittal sections and (B) three-dimensional display showing a linear area of absent tracer uptake from the left renal hilum into the parenchyma, with an interruption of the rim of cortical uptake.

on SPECT changed to normal on RSPECT and 12 of 13 equivocal regions on SPECT changed to 7 normal and 5 abnormal on RSPECT. Buscombe et al. (*11*) found that with a surface rendered three-dimensional display they were able to detect more renal cortical scars than on conventional planar images or on SPECT displayed as slices.

A recent study of Giblin et al. (*12*) on piglets proved SPECT to be 97% sensitive and 93% specific in providing the diagnosis of acute pyelonephritis. The SPECT findings correlated precisely with the extent and severity of histopathological cortical involvement in the acute pyelonephritic process. Using the same experimental model, similar findings were observed by Majd et al. (*13*).

Despite this experimental evidence, it is not obvious that these data simply can be extrapolated to humans. In fact, the renal parenchyma is rather heterogeneous, the number and distribution of the columns of Bertin differ within the same person and from person to person, and the cortical thickness is not equal throughout the whole kidney creating opportunities for false-positive reporting (*14*).

It appeared that studies on normal human kidneys would provide better information about the possible artifacts inherent in kidney SPECT. One possible approach was the study of the contralateral side of a unilateral renal disease. This approach might be criticized, for instance, since a bilateral involvement consecutive to vesicorenal reflux and/or infection cannot always be discarded.

In our study even a retrospective analysis of the planar scintigraphy did not reveal any equivocal image. Several SPECT images could be interpreted as abnormal, as illustrated in Figure 1. Two prominent columns of Bertin, lying close together, make the contrast with the cortex in between so striking that this can be interpreted as a focal defect. Moreover, partial volume effect may, at least in part, explain the cortical defects.

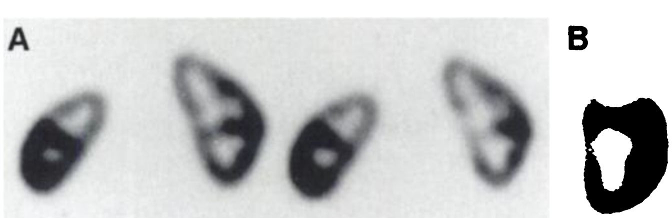

FIGURE 3. (A) Non-reoriented coronal slices and (B) reoriented coronal tomographic section. Cortical rim at the right upper pole with decreased uptake compared to the lower pole.

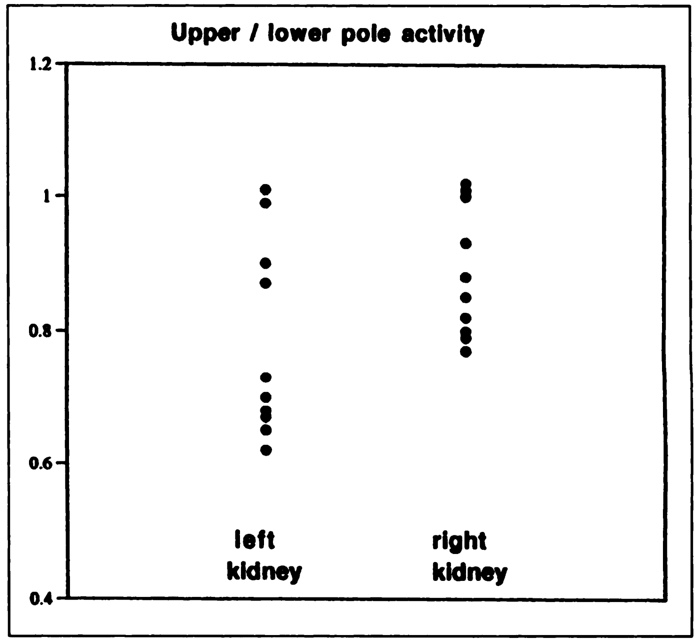

FIGURE 4. Quantitative evaluation of the maximal upper and lower pole activity on the reoriented coronal slices. The ratio of maximal cortical uptake between the two poles revealed differences as high as 35%.

The linear area of absent tracer uptake illustrated in Figure 2 probably corresponds to the anatomical variant described as the interrenicular septum by Rossleigh (*15*), using a one-headed camera.

Our results revealed a high percentage of kidneys (mainly left kidneys) with hypoactive upper poles which, in a context of urinary tract infection, would strongly suggest renal involvement. We do not have a clear explanation for this observation which may be related to variations of the relative parenchymal mass. Attenuation artifacts can play a role, but one would expect these artifacts to be more important on the side of the liver than on the side of the spleen.

CONCLUSION

In this study of normal healthy volunteers, abnormalities were detected in several of the examined kidneys. Because of the heterogeneous and variable configuration of the cortical structures of the kidney, one should be careful in interpreting renal SPECT images. Normal anatomical variants should be recognized and not interpreted as renal lesions.

REFERENCES

1. Höhne KH, Bernstein R. Shading 3-D images from CT using gray-level gradients. *IEEE Trans Med Imaging* 1986;MI-5:45–47.
2. Tarkington MA, Fildes RD, Levin K, et al. High-resolution single-photon emission computerized tomography (SPECT) technetium-99m-dimercaptosuccinic acid renal imaging: a state of the art technique. *J Urol* 1990;144:598–600.
3. Joseph DB, Daniel DW, Young W, Jordon SP. Renal cortical scintigraphy and single-photon emission computerized tomography (SPECT) in the assessment of renal defects in children. *J Urol* 1990;144:595–597.
4. Itoh K, Asano Y, Tsukamoto E. Single-photon emission computed tomography with Tc-99m-dimercaptosuccinic acid in patients with upper urinary tract infection and/or vesicoureteral reflux. *Ann Nucl Med* 1991;5:29–34.
5. Vandevivere J, Melis K, Dobbeleir A. Tc-99m-DMSA renal scan: high-resolution SPECT images using a three-head rotating gamma camera [Abstract]. *J Nucl Med* 1993;33:1021.
6. Mouratidis B, Ash JM, Gilday DL. Comparison of planar and SPECT ^{99m}Tc-DMSA scintigraphy for the detection of renal cortical defects in children. *Nucl Med Commun* 1993;14:82–86.
7. Cooper JA, Martin EL, Jayanthi VR, Cromie WJ. SPECT imaging with ^{99m}Tc-DMSA for detection of renal scars in children with vesicoureteric reflux [Abstract]. *J Nucl Med* 1993;34:51P.
8. Kim SB, Lee MH, Song JH, et al. Triple-head SPECT imaging with technetium-99m-DMSA in adult patients with urinary tract infection [Abstract]. *J Nucl Med* 1993;33:991.

9. Moon DH, Ryu JS, Lee MH, et al. Clinical value of DMSA planar and single-photon emission computed tomography as an initial diagnostic tool in adult women with recurrent acute pyelonephritis. *Nephron* 1994;67:274–279.
10. Rehm PK, Atkins FB, Tall JG, Ziessman HA. SPECT technetium-99m-DMSA renal scans: comparison of native versus reoriented axes [Abstract]. *J Nucl Med* 1993;34: 227P.
11. Buscombe JR, Hilson AJW, Hall ML, et al. Looking for renal scars with technetium-99m-DMSA SPECT: is it worth the effort? [Abstract]. *J Nucl Med* 1993;34:138P.
12. Giblin JG, O'Connor KP, Fildes RD, et al. The diagnosis of acute pyelonephritis in the piglet using single-photon emission computerized tomography dimercaptosuccinic acid scintigraphy: a pathological correlation. *J Urol* 1993;150:759–762.
13. Majd M, Rushton G, Chandra R, et al. Technetium-99m-DMSA renal cortical scintigraphy for the detection of acute pyelonephritis in piglets: comparison of planar and SPECT imaging. *Eur J Nucl Med* 1994;21:343.
14. Williams ED. Renal single-photon emission computed tomography: should we do it? *Semin Nucl Med* 1992;22:112–121.
15. Rossleigh MA. The interrenicular septum. A normal anatomical variant seen on DMSA SPECT. *Clin Nucl Med* 1994;19:953–955.

Technetium-99m-DMSA Renal SPECT in Diagnosing and Monitoring Pediatric Acute Pyelonephritis

Tzu-Chen Yen, Wei-Perng Chen, Shu-Lian Chang, Ren-Shyan Liu, Shin-Hwa Yeh and Ching-Yuang Lin
Department and Division of Nuclear Medicine and Department and Division of Pediatrics, Veterans General Hospital-Taipei and School of Medicine, National Yang-Ming University, Taipei, Taiwan

This study compares the sensitivity of ^{99m}Tc-dimercaptosuccinic acid (DMSA) renal SPECT with planar scintigraphy, concluding the importance of ^{99m}Tc-DMSA renal SPECT for the early diagnosis of acute pyelonephritis (APN) in patients under 3 yr of age. **Methods:** Twenty-seven children under 3 yr of age, with clinical and/or laboratory suspicion of APN, were investigated. All ^{99m}Tc-DMSA renal SPECT and planar images and voiding cystoureterogram (VCUG) were obtained within 3 days of hospitalization. **Results:** In the first examination, renal cortical defects were detected in 23 patients (42 kidneys) with SPECT and in 9 patients (11 kidneys) with planar scintigraphy. One year after treatment, constant renal cortical lesions were observed in 11 patients (14 kidneys) with SPECT and 4 patients (4 kidneys) with planar scintigraphy. The high grades of vesicoureteral reflux (VUR) (grade $\geq$3) correlate better with APN diagnosed by SPECT (34 kidneys) than by planar scintigraphy (8 kidneys). Multiple renal cortical defects (number of lesions $\geq$4) were only seen in patients under 1.5 yr old and none of those with a negative ^{99m}Tc-DMSA renal SPECT had a positive ^{99m}Tc-DMSA renal planar scintigraphy at any time. There is a significant difference ($p < 0.05$) between the diagnostic ability of these two methods of examination. **Conclusion:** Our results suggest that ^{99m}Tc-DMSA renal SPECT should be used, where possible, instead of planar DMSA in routine examination of children with clinical suspicion of APN, especially for those under 3 yr of age.

Key Words: pediatric acutepyelonephritis; SPECT; technetium-99m-dimercaptosuccinic acid

J Nucl Med 1996; 37:1349–1353

Urinary tract infection (UTI), the admission diagnosis for about 140 patients hospitalized per year in the Veterans General Hospital-Taipei, is most often due to Escherichia coli infection of the renal parenchyma and collecting system. Although certain characteristics may help to differentiate acute pyelonephritis (APN) from cystitis, their clinical presentations are often similar. Sometimes it is difficult to distinguish between them.

The diagnosis of APN is very important for pediatric patients, especially for neonates and infants, because improper or delayed treatment of APN is often associated with the development of renal scarring and/or chronic pyelonephritis, evidenced by calyceal distortion of intravenous urography (IVU), repeated bouts of UTI, renal hypertension and even renal failure (*1*). It has been reported that in children, APN will cause renal scarring in 47% to 68% of patients through different modalities of imaging study (*2*) and recurrent episodes of APN will cause in one-third of patients progressive renal scarring, contracted, distorted or small kidneys (*3*). In most children, diagnosing APN does not require complex and expensive procedures. From our previous study, ^{99m}Tc-dimercaptosuccinic acid (DMSA) renal SPECT scan has been found to be a useful diagnostic tool in children ($\geq$3 yr old) with APN (*4*). However, in neonates and infants with equivocal or negative urine cultures or with recurrent cystitis and no evidence of pathologic vesicoureteral reflux (VUR) proved by voiding cystoureterogram (VCUG), asserting or ruling out this diagnosis is mandatory for effective management. In addition, following and monitoring the effect of treatment are also very important for determining the prognosis of patients after APN.

Recent studies have compared the sensitivity and specificity of various imaging modalities, including the ^{99m}Tc-DMSA renal scan, IVU, CT, ultrasonography (US) and MRI in detecting renal lesions in children. SPECT renal imaging has proved to be superior to the other diagnostic modalities (*4–10*). However, to the best of our knowledge, no report is known that uses the ^{99m}Tc-DMSA renal SPECT technique to diagnose and monitor APN in infants. In this research, we extend our previous studies using both ^{99m}Tc-DMSA renal planar scintigraphy and SPECT to diagnose and follow up infants with a clinical suspicion of APN (*4*) and compare the results with the VCUG.

METHODS

Patients

This study was performed between August 1, 1992 and August 30, 1994. Three hundred and nine patients were referred to by Pediatric Nephrologists of the Veterans General Hospital-Taipei. APN was defined as being present if they had all of the following: there was fever ($\geq$38.5°C), pyruia (WBC counts/HPF $\geq$10), a positive urinary culture and/or a positive blood culture. Twenty-seven of them were under 3 yr of age (from 1 wk old upward) and clinically and/or laboratory diagnosed to have APN. The other 282

Received June 12, 1995; revision accepted Dec. 13, 1995.
For correspondence or reprints contact: Dr. Tzu-Chen Yen, Department of Nuclear Medicine, Veterans General Hospital-Taipei, Taipei, Taiwan.