Procedures of Choice in Renal Nuclear Medicine

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The uronephrologic applications of nuclear medicine have reached a stage of maturity where procedures of choice for many specific clinical problems can be identified. This review attempts to achieve this aim as objectively as possible. *It must be emphasized that the opinions expressed here are those of the author and in many areas there may be a lack of consensus.*

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The most important concept in studying the kidney is a recognition of the intimate relationship between structure and function. Although procedures which are primarily functional and procedures dependent on imaging are discussed separately here, no renal study can be evaluated properly without considering its physiologic basis. Table 1 lists the major radionuclide procedures available in uronephrology.

Among the clearance methods, the continuous infusion technique has been and continues to be a major method for investigational studies where accurate and precise measurements of renal function are needed. The use of continuous infusion clearance in clinical practice is limited and will not be discussed here. The single injection clearance methods offer the great advantages of simplicity, ease of performance, low radiation dose, and reasonable accuracy.

Radiorenography has evolved into a complex technique. Captopril renography is being used with increasing frequency while exercise stress renography may prove to be of value in the future. Among the pharmaceuticals for renal imaging, ^{99m}Tc-glucoheptonate and ^{99m}Tc-DMSA have very different mechanisms of renal handling than ^{99m}Tc-DTPA (excreted by glomerular filtration), and ^{99m}Tc-MAG$_3$ and ^{131}I-hippuran (excreted primarily by tubular secretion). Technetium-99m-MAG$_3$ has been approved recently by the FDA and is available for routine applications, although pediatric use of this agent has not yet received approval.

The radionuclide cystogram has achieved widespread application in the evaluation of ureterovesical reflux. The radionuclide method for measuring residual urine, which was described more than 20 years ago, has not achieved general use and may now be largely obsolete. Testicular imaging is established in genitourinary imaging while the application of radionuclides to studies of patients with impotence and related diseases is rapidly moving toward clinical practice and will likely expand this area of use in the future.

The specific pathologic conditions in which nuclear medicine may play a role are listed in Table 2.

In reviewing procedures of my choice in renal nuclear medicine, it is necessary also to evaluate these procedures in relation to radiographic and other diagnostic imaging procedures. The complementary modalities to be considered are ultrasound, urography, angiography, and computed tomography (CT). At this time, there are few data that would support the utilization of magnetic resonance imaging (MRI) in the routine clinical evaluation of the kidneys and urinary tract. This area of application of MRI has been a great disappointment so far, but continues to be an area of active investigation.

RADIOPHARMACEUTICALS FOR RENAL STUDIES

The radiopharmaceuticals that have been used for kidney studies are shown in Figure 1.

Glomerular Filtration Rate

The radionuclide agent of choice for an extremely accurate measurement of the glomerular filtration rate (GFR) is ^{51}Cr-EDTA (*1*). This agent is not available in the U.S., but it is widely used in Europe. The clearance of ^{51}C-EDTA is virtually identical with the clearance of inulin, therefore, it is a true GFR marker. In the U.S., ^{131}I-iothalamate has been used in its place. Technetium-99m-DTPA has a clearance rate approximately 5% less than that of inulin (*2*), which usually is an acceptable error in clinical practice. The error of serum creatinine is in the range of 10% or 15% in estimating GFR and may be greater in renal failure. *Technetium-99m-DTPA yields an estimate of the GFR within 5% of the true GFR. It is inexpensive, has a low radiation dose, and, most importantly, it can be used for renal imaging, making it the GFR agent of choice overall in clinical nuclear medicine practice.*

Tubular Secretion

Iodine-131-hippuran is currently the agent of choice for estimating effective renal plasma flow (ERPF). Iodine-123-

TABLE 1
Uronephrologic Procedures in Nuclear Medicine

1. Clearance Methods	5. Radionuclide cystogram
A. Continuous infusion	A. Residual urine
B. Single injection	B. Ureterovesical reflux
C. Simplified single injection	6. Scintiphotography
D. In vivo camera techniques	A. Individual renal function
	1. ^{131}I-, ^{123}I-hippuran
2. Radioimmunoassay	2. ^{99m}Tc-DTPA
A. Angiotensin	3. ^{99m}Tc-MAG$_3$
B. Renin activity	B. Individual renal mass
C. Aldosterone	1. ^{99m}Tc-DMSA
3. Radiorenography	2. ^{99m}Tc-glucoheptonate
A. ^{99m}Tc-DTPA	C. Perfusion imaging
B. ^{131,123}I-hippuran	1. Any low-dose ^{99m}Tc agent
C. ^{99m}Tc-MAG$_3$	D. Morphology
D. Miscellaneous	1. Renal mass agents
4. Body spaces	7. Renal blood flow
	8. Genital imaging
	A. Penile blood flow
	B. Testicular perfusion

hippuran has a lower radiation dose, and so it is theoretically preferable to ^{131}I, but because of cost limitations and a short shelf life, the ^{131}I agent is the most practical for measuring ERPF. Technetium-99m-MAG$_3$, which has only been available for a relatively brief time in the U.S., may assume a major role in evaluating tubular secretion. MAG$_3$ is significantly different from hippuran in that MAG$_3$ apparently clears at a rate lower than ^{131}I-hippuran (about 80%) because it is not filtered by the glomerulus (*4*). Although it has lower clearance values, MAG$_3$ is taken up in very high quantities, gives excellent renal images, and has moved rapidly into routine practice. The small difference in excretion characteristics may be of value in some situations where it is desirable to evaluate pure tubular secretion. Hepatic excretion of MAG$_3$ is a problem that may interfere with its use in single injection clearances at low levels of renal function. Clearance techniques that include urine collection avoid this problem.

TABLE 2
Nuclear Medicine in Genitourinary Disease

Acute renal failure
Chronic renal failure
Congenital anomalies
Epididymitis
Impotence
Mass Lesions
Pyelonephritis
Quantitation of renal function
Renal perfusion abnormalities
Renal trauma
Renovascular hypertension
Residual urine
Testicular torsion
Transplantation
Ureteral vesical reflux
Urinary tract obstruction
Varicocoele
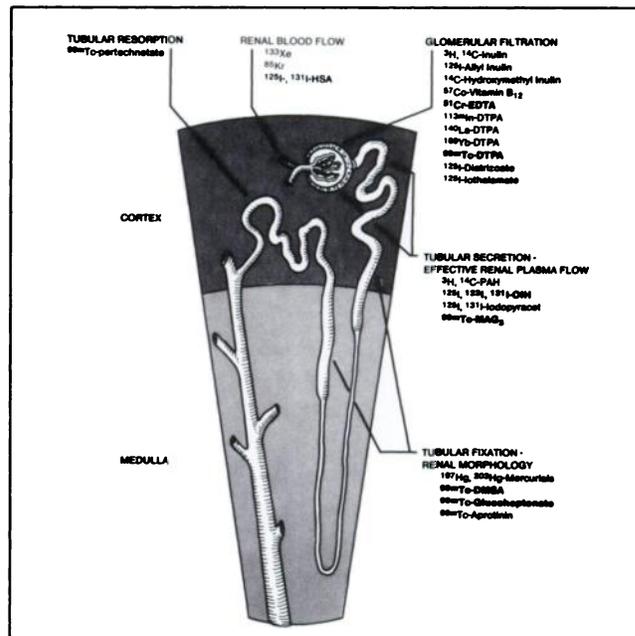
FIGURE 1. Graphic depiction of the areas of the nephron where various radiopharmaceuticals are handled. Those pharmaceuticals that are considered to be agents of choice are shown in bold.

Static Imaging Agents

Technetium-99m-DMSA and ^{99m}Tc-glucoheptonate are the two major agents available for renal parenchymal imaging. These two radiopharmaceuticals are very different. A significant portion of glucoheptonate is filtered (*5*), so that in patients with urinary tract obstruction, the accumulation of glucoheptonate in the collecting system can present a problem in interpreting parenchymal images. In patients without urinary tract obstruction, the filtered component is not a problem and it can be advantageous in providing additional information about the collecting system.

Technetium-99m-DMSA is handled by a very different excretory mechanism (*6*). Glucoheptonate shares the enzyme system for para-amino-hippuric acid and ^{131}I-hippuran in the proximal tubules, while ^{99m}Tc-DMSA is excreted by a different process. It is concentrated to a greater extent (about 40% of it is accumulated in the kidneys) and as a result ^{99m}Tc-DMSA delivers a much higher radiation dose (per MCi administered) to the kidney than ^{99m}Tc-glucoheptonate. If a renal perfusion study is needed in conjunction with a static imaging study, ^{99m}Tc-glucoheptonate is suitable because of the lower radiation dose. Technetium-99m-DMSA should not be used for flow studies, but it is an ideal agent for extremely detailed renal cortical images. *The best way to minimize radiation dose and perform a flow study in patients in whom perfusion imaging is needed in concert with static imaging is to do a flow study with ^{99m}Tc-DTPA followed by a static study with ^{99m}Tc-glucoheptonate, or if very fine resolution is needed,*

followed by ^{99m}Tc-DMSA. Quantitative separated renal function studies may be performed with DMSA. Many centers use a single dose of glucoheptonate for the perfusion and imaging study. A number of centers use glucoheptonate instead of DMSA for quantitative imaging.

Gallium may be considered as a renal agent when used in studying pyelonephritis or renal abcess. Monoclonal antibodies and indium-labeled white cells have not proved practical for renal imaging and are not discussed here, although they are still being actively investigated.

CLEARANCE METHODS

The clearance techniques currently available include: compartmental analysis methods, which require four to six blood samples; simplified models (single-compartment), which require only two samples; a further simplified model, which utilizes one sample; and several gamma camera external counting methods, which require no plasma samples. The question repeatedly asked is: "Which one of these techniques should I use?" Besides these popular methods, numerous others have been described. All of these techniques work, but they differ in their advantages and disadvantages.

Multi-compartmental systems (more than two compartments) add little or nothing to the accuracy of clearance techniques. The two-compartment model appears to provide the most accurate measurement of renal function when an agent is used for single injection clearance and requires about six blood samples. Technetium-99m-DTPA or ^{131}I-hippuran may be used for accurate estimates of the clearance of these agents (7), but the technique is probably more accurate than necessary for most clinical situations. Although techniques requiring urine collection avoid the assumptions of disappearance methods, they do not obviate urine collection which is cumbersome. Therefore, they will not be discussed further.

The simplified model has a role in clinical practice and so do the single-sample and the gamma camera methods. The two-sample method is quite simple. Two blood samples are obtained for ^{131}I-hippuran, one at about 30 min and one at 40 min. The rate of disappearance of the isotope is used to estimate renal clearance, which is calculated from the product of the slope of the exponential disappearance and the volume of distribution (8). The single-sample method requires only a single blood sample drawn at about 44 min (for hippuran). This sample is assumed to fit to a known parabolic or exponential function to calculate the clearance. The relationship between the one-sample clearance method and the two-sample clearance method (Fig. 2) is excellent. If an adult study requires measurement of ERPF, then my procedure of choice is a single 44-min sample of plasma fitted to the Tauxe equation. This method yields accurate measurement of ERPF in adults, but it may not be reliable in children.

Several investigators are working now on the application of the single-sample technique to measure GFR using
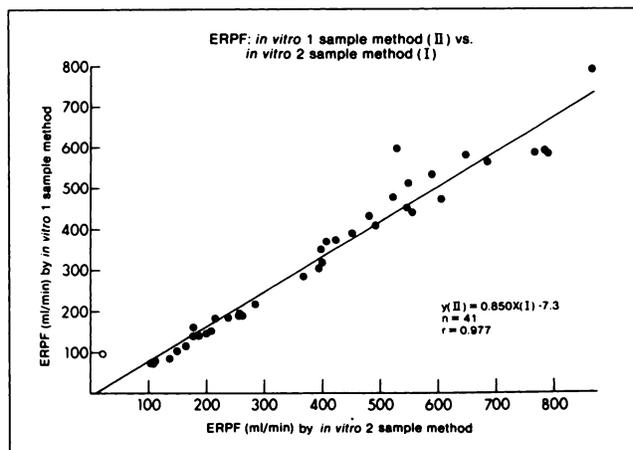
FIGURE 2. Correlation between measurements of effective renal plasma flow using the in-vitro one-sample method versus measurements using the in-vitro two-sample method. The correlation is excellent supporting the close relationship and accuracy of both methodologies. (Reprinted with permission from reference 28, Fig. 2).

^{99m}Tc-DTPA. There is not yet a body of data as extensive for GFR measurements as currently exist for ERPF measurements using one sample. At this time, a conservative approach calls for measurements of GFR using a two-sample method drawing the plasma samples at about 120–180 min if possible but no earlier than 100 min after injection (10). This approach is applicable to children, although the best time to draw the samples is widely debated.

The one-sample method does not appear to be applicable for use in children due to the rapidly changing relationships in body compartments and body size and in renal function itself. The assumptions needed for a single-sample technique may be erroneous unless a curve is constructed for every age or level of renal function. Therefore, in studying children, the two-sample method remains the technique of choice. Table 3 lists the normal values for renal function at several age levels.

Figure 3 shows the correlation between the two-sample method and external measurement of ERPF. Considerable scatter also is shown. In switching from a blood sampling technique to an external counting technique, a wider range of error is introduced. Any external counting technique will be significantly less accurate than a technique using blood sampling.

Among the external counting techniques for evaluation of individual renal function, the initial slope method has not been as reliable as the integral method in my experience. The results appear to worsen with background subtraction. The great variability of the slope method and the error introduced by background subtraction (although the literature suggests otherwise) are serious limitations (11). The integral method for individual renal function is my procedure of choice. It should be emphasized that there are many strong proponents of the slope method whose ex-

| Age	C_{In}	C_{PAH}
<3 mo	16–60	50–86
6–8 mo	60–120	70–109
20–29 yr	123 ± 16	638 ± 195
30–39	119 ± 11	592 ± 123
40–49	121 ± 23	494 ± 135
50–59	99 ± 15	
80–89	65 ± 20	

Table modified from references 30 and 31.
Legend: The clearance values listed above were completed from several sources in the references noted. Note the increasing values with age 20–29 yr followed by a decline representing growth and maturation into adulthood and then a progressive loss of functioning nephrons.

periences differ from ours. Our studies suggest that the use of background subtraction introduces more problems than it solves at relatively good levels of renal function. Recently, Piepsz published a technique using multiple regions of interest, combined to do background subtraction (12) but this has not been confirmed. Values of separate renal function in patients with relatively good renal function, in my experience, are less reproducible when background subtraction is applied. It is not known what the best background region is, and there probably is no way to choose the true background. Results in patients with reasonable levels of renal function are highly reproducible if integral methods are used without background subtraction. It is the reproducibility of the results that usually is most important clinically in following patients to see whether they have significant changes in renal function. I recommend the integral of the count rate between 1 and 2 min or between 1.50 and 2.50 min (13).

Another major problem with quantitation of renal function is due to variability of renal depth. Maneval has published data showing that in children there is significant variability in renal depth (14) among and between the kidneys. Assumptions about kidney depth lead to error, as do the various equations to correct for depth. The formula correction for renal depth is not accurate. If individual renal function is to be measured most accurately, we use the integral technique with no background subtraction and, if possible, correct for measured renal depth. This may be done with a camera technique using a lateral view or a geometric mean. The best possible but least practical way to correct for depth is to measure the true renal depth with ultrasound. Regardless of the approach used, renal depth is a source of error and tends to make the measurement of individual renal function less accurate but not less precise. The standard error of the estimate in external counting techniques is about 20%. This is a significant error, but it is usually acceptable within clinical settings where no other method yields individual renal function. In the future, there may be more accurate methods of measuring individual renal function with camera methodology. Paramora (15) compared renal volume estimated from SPECT versus DMSA uptake and demonstrated excellent preliminary results.
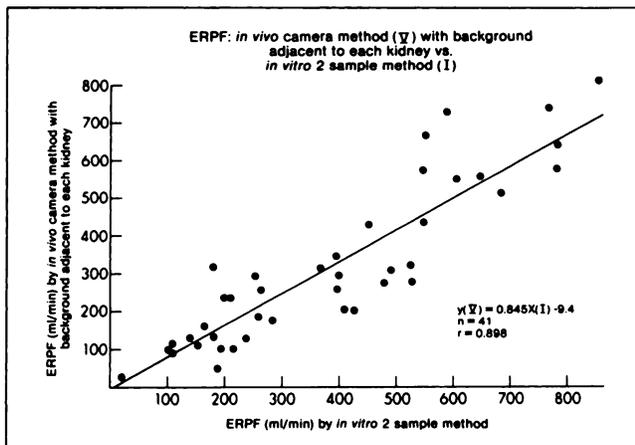
FIGURE 3. Correlation between the in-vitro two-sample method and in-vivo methods for measuring effective renal plasma flow with external camera techniques. Although the correlation is excellent, notice the very wide scatter compared to the scatter shown in Figure 2. The accuracy of the in-vivo technique is considerably less than that of the in-vitro technique because of the problems posed by variations in renal depth, background contribution, and the numerous assumptions which have to be made for the technique. (Reprinted with permission from reference 28, Fig. 5).

IMAGING TECHNIQUES

Congenital Anomalies and Mass Lesions

Nuclear medicine has an important and a complementary role with radiographic techniques in the evaluation of congenital anomalies of the kidney. An important area is the differentiation between renal mass and a hypertrophied renal column or unusual shape. Although oncocytoma has been reported to concentrate hippuran (16), tumors of the kidney rarely concentrate renal imaging agents. No malignant tumor has demonstrated uptake. The differential diagnosis between hypertrophied column, congenital malformation and tumor may not be resolved with ultrasound. The procedure of choice in the differential diagnosis between hypertrophied column, unusual renal shape, and intrarenal tumor is a glucoheptonate or DMSA scan. Ultrasound provides complementary information.

Among the other congenital anomalies, horseshoe kidney, which is difficult to image by radiographic techniques, may be evaluated with radionuclides. It may be determined easily with radionuclide imaging if the tissue overlying the spine represents functioning renal parenchyma or is simply a fibrous band.

Other mass lesions are not in the domain of nuclear

medicine at the present time. There may be future potential for nuclear medicine's role in tumor evaluation. In a study by Williams, which evaluated the use of SPECT to determine mass lesions of the kidney, small lesions representing true-positive findings significantly increased with tomography compared with planar imaging (*17*). Nuclear medicine's role in neoplastic disease of the kidney currently is only secondary.

Urinary Tract Obstruction

Nuclear medicine is the technique of choice for evaluating the patient once the anatomic diagnosis of ureteral or pelvic dilatation has been made using a radiographic procedure or ultrasound. The information not obtained by ultrasound or urography is the functional significance of the observed dilatation. The most important consideration may be to determine if the lesion represents significant obstruction that will have an adverse effect on overall renal function. Nuclear medicine techniques to determine the individual renal function provide an important baseline and a sensitive follow-up.

The Whitaker test, for example, yields information very different from that provided by scinti-imaging. Some physicians believe that the Whitaker test is all that is needed to evaluate obstruction and to determine its functional significance. The Whitaker test involves intubation of the kidney and the infusion of saline at a controlled rate (usually about 10 ml/min). The normal rate of the urine flow is only 0.5 ml/min and may reach levels of 10 ml/min only during periods of extreme diuresis. So the urinary tract is severely stressed by the Whitaker test. I believe that the significant question is not whether the urinary tract can deal with a high urine flow rate, but whether the urinary tract under normal circumstances is handling the volume load presented to it and whether there exists an adverse functional effect for the kidney's inability to handle large volumes of urine flow.

Diagnosis of Obstructed Versus Nonobstructed Dilatation

The differential diagnosis of the significance of ureteral dilatation is best evaluated with the lasix renogram. O'Reilly has now defined his procedure of choice (*18*). In performing lasix renography, I prefer his approach which is to read a baseline renogram, and if there is evidence of a delay in the excretion of the radiopharmaceutical to administer the lasix 15 min prior to a repeat renogram. Several alternative approaches appear to be reliable, but they have not had as much controlled study. Most cases will show a clear cut obstructive or nonobstructed curve using this approach, and the number of equivocal responses appears to be reduced. It is important that if an equivocal response is obtained the interpretation should be exactly that. The patient should be studied again in 3–6 mo to evaluate any change in renal function. If renal function is stable, there is no urgency to intervene.

If the urinary tract is clearly obstructed and the patient cannot handle a significant load of fluid, then there may be an indication for surgical correction. In patients with markedly reduced renal function, lasix may not cause a diuresis and this should always be kept in mind as a potential source of error. In this situation the only test available to determine the integrity of the urinary tract may be the Whitaker test. Lasix renography with ^{99m}Tc-MAG$_3$ appears to yield results that are quite similar to ^{131}I-hippuran (Fig. 4). Technetium-99m-MAG$_3$ has the advantage of yielding excellent images of the collecting system. Technetium-99m-DTPA is an alternative agent, but it has a higher background.

There is an ongoing study by the pediatric nuclear medicine group to evaluate lasix renography in children. The problem they have encountered is the increasing number of neonates born with antenatal diagnoses of dilatation of the urinary tract as a result of the increased use of ultrasound in these patients. Ultrasound only shows
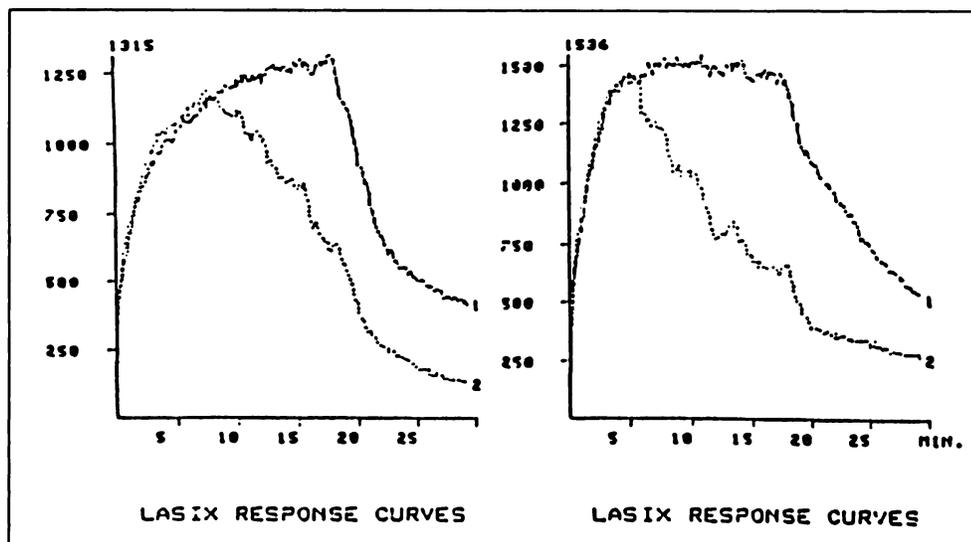
FIGURE 4. Lasix response curves in a patient who has received an intravenous injection of ^{99m}Tc-MAG$_3$ (left) and a second injection of ^{123}I-hippuran (right) are shown above. Lasix was administered in each case at 18 min and the two curves are quite similar. This is a response suggestive of nonsignificant obstruction. (Reprinted with permission from Reference 29).

dilatation, but it does not differentiate if the dilatation is functionally significant. Neonates lack maturity of the kidney and so during the first 4–6 wk after birth, the response to lasix may be unpredictable and the failure of radioactivity to wash out of the urinary tract after administration of lasix, theoretically, may not be due to obstruction of the urinary tract but may be a reflection of the immaturity of the kidney. During the first 2 wk of life, diagnoses of obstruction using the lasix washout should be interpreted with caution, and studies of neonates should be delayed as long as practical. These recommendations may change when the pediatric study data are available.

Renal Failure

The azotemic patient with renal failure is at increased risk of losing some renal function as a result of being given contrast media. This is particularly true in the diabetic patient. *Diabetics with elevated serum creatinine levels should be studied first with nuclear medicine techniques or ultrasound and only given contrast if it is required for definitive diagnosis.* Even non-diabetic patients with elevated creatinine may show a further increase in creatinine after urography.

The choice between ultrasound and nuclear medicine depends upon the specific question being asked. Patients whose kidneys do not visualize with hippuran are relatively uncommon, and this has important prognostic significance.

In a study of 28 patients with nonvisualization, 16 had chronic renal disease and required dialysis within 6 mo, 5 had obstruction, 4 of these agreed to treatment and improved, and 7 had acute renal failure and died (*19*). Nonvisualization with hippuran in the absence of obstruction is a poor prognostic sign. In chronic renal failure it suggests that the patient will need dialysis in a few months; in acute renal failure the chance of death is high. It is extremely important to note that in the presence of obstruction, the patient may have recoverable renal function.

The newer cameras may cause problems with ^{131}I-hippuran imaging, and the technique has to be carefully standardized. An example of nonvisualization with hippuran is shown in Figure 5. After about 3 mo of nephrostomy drainage, the patient had adequate renal function to sustain life. Therefore, *if a new patient presents with chronic renal failure, the patient can either go directly to ultrasound to rule out obstruction, or the patient can have a renal scan. If the patient's kidneys are visualized, there is a potential for recovery, but obstruction still needs to be ruled out. If there is no visualization an ultrasound study is mandatory.* The absence of obstruction and renal visualization suggests a poor prognosis. *The presence of obstruction is an indication for surgical intervention even if the kidney does not visualize with hippuran.* These statements are based on experience with ^{131}I-hippuran. Technetium-99m-MAG$_3$ has not been studied sufficiently to make a general statement about nonvisualization with this agent. Other radiopharmaceuticals have been used but they have not been studied as extensively.

Nuclear medicine can provide a relatively specific diagnosis in the patient with chronic interstitial nephritis. The typical appearance of chronic renal failure with a delayed uptake is shown in Figure 6. There is activity in the bladder, however, unlike acute renal failure, at 24 hr there is virtually no activity left in the kidney. The diagnosis is made by the administration of gallium which at 72 hr shows intense uptake. *Intense symmetric uptake of gallium 72 hr or more after a renal scan in a patient with renal failure is highly suggestive of a diagnosis of interstitial nephritis (20).* The gallium scan cannot reliably be interpreted earlier than this because with azotemia there is a delay in the excretion of gallium by the kidney and the uptake may be relatively intense.

FIGURE 5. (A) A series of images taken after the injection of ^{131}I-OIH in a patient with no evidence of renal function is shown. The kidneys cannot be identified with any certainty in any of the images. (B) Following several weeks of catheter drainage, the ^{131}I-OIH study is repeated in the same patients after the bilateral nephrostomy tubes have been removed. Note that now there is significant renal uptake which is seen as early as the 0–3-min image with progression into the collecting system and bladder throughout the subsequent images.
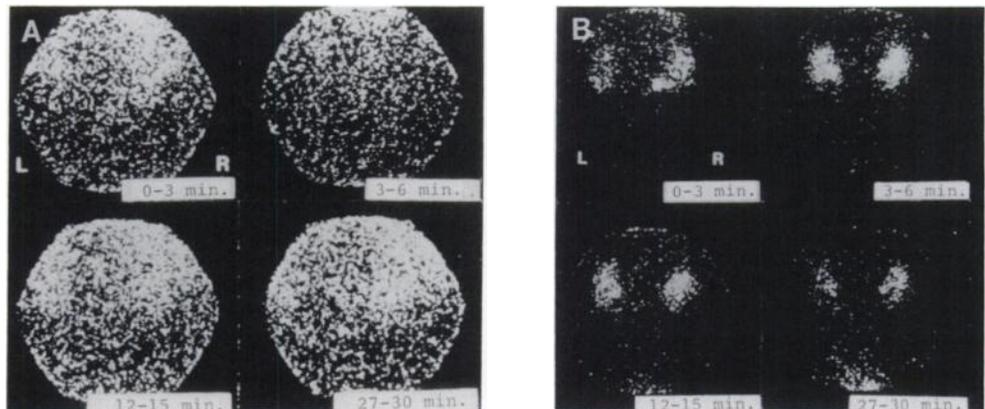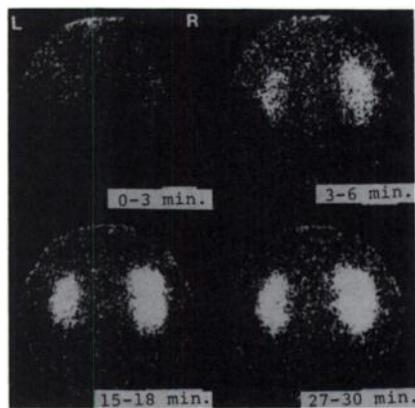
FIGURE 6. A series of images in a patient with chronic renal failure is shown above. Note especially the minimal visualization of the kidney from 0 to 3 min, suggesting a significant delay in uptake, the increased background activity throughout the study and the persistence of activity at 27–30 min, which is a result of the delayed excretion associated with probably a reduced urine flow and some intratubular obstruction.

Infection

Urinary tract infection is an area where nuclear medicine offers unique opportunities that have been largely underutilized. The urogram may appear normal in patients with infection involving the upper urinary tract. The differential diagnosis between cystitis and renal infection is difficult. Handmacher has shown quite clearly that in patients with pyelonephritis, there are areas of non-uptake of DMSA due to the inflammation of the renal parenchyma (21). Glucoheptonate also can be used in a similar manner, and in patients who have abscess or localized infection of the kidney, gallium can be extremely useful. Differentiation of acute renal infection from cystitis can be similarly useful in the patient with chronic disease in whom chronic changes may exist on a urogram (22). *DMSA imaging or glucoheptonate can be used to diagnose upper urinary tract infection. Gallium may be used to to identify an abscess.* These techniques are more sensitive than urography.

Renal Perfusion

Nuclear medicine has a limited role in evaluating renal perfusion. We followed a patient with arterial venous fistula for more than 12 yr until she finally went on dialysis in 1989. It was possible to follow the perfusion of the kidney with technetium flow studies and to avoid the need for repeat arteriography. Her renal function was followed by serial hippuran renograms. I believe that there are relatively few situations where a renal perfusion study is of great diagnostic importance. Arterial venous fistula of the kidney, aortic obstruction, are a few, but *in the vast majority of situations, one could probably not do a flow study and lose little information. Renal transplantation is the primary exception. Flow studies can be performed with* ^{99m}*Tc-DTPA,* ^{99m}*Tc-MAG$_3$ or* ^{123}*I-hippuran.*

Transplantation

Renal transplantation is another area where radionuclides have achieved broad use. Characteristic patterns of rejection and ATN have been described. In ATN, the kidney is well perfused, there is little or no urine formation and moderately good but delayed renal uptake of activity. Rejection is associated with poor perfusion of the kidney, poor renal uptake, but usually continued urine formation. The differential diagnosis of rejection has been complicated by the widespread use of cyclosporin. No reliable technique is routinely available to differentiate transplant rejection from cyclosporin toxicity. *Patency of the anastomosis can be assessed with a perfusion study, level of function with* ^{131}*I-hippuran,* ^{99m}*Tc-DTPA, or* ^{99m}*Tc-MAG$_3$, and in patients suspected of having urinary extravasation, integrity of the urinary tract can be evaluated with* ^{99m}*Tc-glucoheptonate.*

Numerous approaches to evaluating transplants have been reported. These include the use of indium-labeled red blood cells, gallium, and ^{99m}Tc-sulfur colloid. Although I prefer the simple approach outlined above, the literature should be reviewed for alternatives.

Professor Hertil from Frankfurt has obtained anti-T-lymphocyte monoclonal antibody scans of normal transplants with no uptake in the region of the transplant. Intense uptake occurred in patients who had ongoing rejection of the kidney. This is a promising new application of radionuclides (Hertil A, *personal communication*). If these studies are confirmed and if the patients tolerate the agent, this could be an extremely important development in the role of nuclear medicine in renal transplantation.

Renovascular Hypertension

The standard technique for evaluating patients for renovascular hypertension involves combined imaging using either ^{131}I-hippuran or ^{99m}Tc-DTPA and the generation of a time-activity curve to evaluate the relative rate of uptake and disappearance. Normally, the kidney uptake pattern should be symmetrical. Characteristically in a patient with renovascular hypertension, there is a less rapid rate of uptake by the involved kidney and the rate of washout is slower. The disparity between the normal and abnormal kidney depends upon the degree to which the abnormal kidney is affected. Bilateral disease presents a much more complex and unpredictable pattern, especially in the presence of significantly reduced renal function.

Images of the abnormal kidney usually show that it is somewhat smaller, picks up activity less rapidly, and at 27–30 min the image commonly only shows the abnormal kidney, with the normal kidney having cleared. This pattern reflects the physiologic sequence of events in renal artery stenosis where GFR is reduced, there is increased water reabsorption, and therefore there is a reduced rate of delivery of the radioactive material to the kidney and reduced washout from the kidney because of the reduced urine flow rate. The technique is quite accurate with about

an 85% true-positive rate, similar to that reported by McNeil and others for urography (23, 24). The problem is not its ability to detect renal artery stenosis, but rather the high false-positive rate of about 10%, which also is equivalent to the urogram. This results in a large number of false-positives in a disease with a low prevalence. Although the technique has problems, it still is extremely useful in the differential diagnosis of renovascular disease, and radionuclide techniques in particular play an important role in the follow-up of patients if an intervention is performed. *In determining whether a patient should have digital subtraction angiography, the radionuclide technique helps to specify a patient population with a greater probability of disease.* Once the disease is diagnosed, angiography then can be performed to detect renal arterial lesions. *Subsequently, the renogram can be used for follow-up using the initial test as the baseline, thus avoiding the necessity for postintervention angiography in determining the adequacy of the intervention in restoring renal function.* This is a highly cost-effective and useful approach that reduces patient exposure to contrast media toxicity. However, reducing the false-positive rate in screening for renovascular hypertension is still desirable. The captopril renogram may have potential for accomplishing this goal.

The generation of endogenous angiotensin within the glomerular capillary leads to post-glomerular vasoconstriction in patients with renovascular hypertension. Because perfusion pressure is reduced by renal artery stenosis, there is a tendency for GFR to fall, but by further constricting the post-glomerular arteriole, the pressure gradient across the glomerulus is maintained and GFR is restored toward normal. If a patient with renovascular hypertension is given captopril or another converting enzyme inhibitor, the concentration of angiotensin in the glomerulus falls and the compensatory effect of constriction of the post-glomerular vessel is lost. This results in relative dilatation of the efferent arteriole with a reduction in the transcapillary gradient and a fall in GFR. This fall in GFR may be detected with radioisotope techniques.

With the reduction of GFR after captopril, there is a dramatic worsening of function as shown by the renogram curve, and this response to captopril may be interpreted as a positive and relatively specific test for renovascular hypertension. Parameters which appear to be of use in captopril renography include global renal function measurement, relative renal function, urine specific gravity, measurement of the blood pressure, and numerical analysis of the curves. The curves in patients with essential hypertension show little or no change post-captopril (25). In about 20% of patients without renovascular hypertension, the scinti-images may reveal pelvic retention. This should not be confused with a positive test and cortical regions of interest should be generated to determine if these curves are more normal. Inspection of the scinti-images and generation of cortical regions of interest appears to provide sufficient information to prevent erro-

neous interpretation of the renogram. Sfakianakis has suggested that errors in interpretation may be avoided by giving all patients lasix as well as captopril (26). *The renogram is a highly cost-effective procedure for screening for renovascular hypertension. Presently, my procedure of choice for captopril renography and for differential diagnosis of renovascular hypertension is: to stop diuretics 5 days prior to the test; stop other medications as soon as possible; enalapril at least 3 days before; captopril at least 2 days before; hydrate the patient in the department; give 25 mg of captopril (some centers use 50 mg)—(crush the tablet) 1 hr before the renogram (or enalaprilat i.v. 15 min before). The patient must be fasting; do curves plus images; use either DTPA, hippuran, or MAG$_3$ according to your preference; optionally use lasix; if the renogram is abnormal repeat the test without captopril (or enalaprilat) either 6 hr later or the next day.*

Numerous other approaches have been reported (27) and these should be reviewed before making a final choice.

Renal Trauma

Evaluation for renal trauma with nuclear medicine techniques has slackened due to the availability of CT scanners in emergency rooms, but nuclear medicine does have a role in studying the functional consequences of renal trauma and in the follow-up of kidney recovery.

Genital Imaging

Testicular scanning for torsion and epididymitis is the procedure of choice. Ultrasound does not approach the reliability of nuclear medicine techniques except in a few small studies. Nuclear medicine should not delay surgery but should simply help the surgeon make a decision.

During the next few years, it appears that evaluation of impotence with various nuclear medicine techniques will begin to become part of the armamentarium and may compete with selective arteriography because of its less invasive nature and the more quantitative information provided.

Although available for many years, residual urine estimates have been much underutilized in spite of their great accuracy. *Because of the dangers and inconvenience of catheterization, the isotope test is preferable for evaluation of residual urine coupled with a renogram to evaluate the upper tract, especially in patients with suspected prostatic disease.* The increased availability of ultrasound to measure residual urine may make this procedure obsolete except in patients who are being imaged.

For vesical ureteral reflux, the radiographic procedure should be the first line of diagnosis. Because of the low radiation dose and high sensitivity, *a radioisotope cystogram is the procedure of choice for follow-up and evaluation of surgical results.* Indirect cystography has its advocates, but it has not been studied as well nor is it as direct.

FUTURE DEVELOPMENTS

Some years ago, I proposed several areas for future development in renal nuclear medicine. We already have

made considerable progress towards immunologic imaging of the kidney, definition of three ideal pharmaceuticals for GFR, ERPF and renal mass, and the use of SPECT for quantitation of renal mass. For example, immunologic imaging has been implemented for transplantation, early studies for quantitation of renal mass with SPECT have been done, and presently we have ^{99m}Tc-DTPA for GFR, ^{131}I-hippuran for ERPF, and ^{99m}Tc-DMSA for renal mass, with very active work underway to identify further agents. The exact role of ^{99m}Tc-MAG$_3$ will become clear in the near future, although its role as a pure tubular agent is unique. We desperately need convincing and carefully carried out efficacy studies of nuclear medicine techniques versus CT, ultrasound, and MRI. We need to define where nuclear medicine techniques fit in definitively with relation to ultrasound and CT, since there are many centers that utilize these techniques rather than nuclear medicine. Nuclear medicine has something unique to offer and hopefully these remaining problems will be resolved over the next several years. There has never been as much attention to renal studies in nuclear medicine as we are currently witnessing.

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