Scintiphotography in Evaluation of Renal Transplants

HALCOTT T. HADEN, M.D.

Associate Professor of Radiology and Medicine, Chief, Nuclear Medicine Section, McGuire VA Hospital, Richmond, Virginia

Renal transplantation has progressed from the research stage to become a standard clinical procedure. Although still generally limited to large medical centers, renal transplants are regularly done in over 135 hospitals in the United States. In 1972, approximately 2,600 renal transplants were recorded in the United States by the Renal Transplant Registry (1). Approximately 65% of these were cadaver donors and 35% living donors.

The kidney transplant recipient is subject to a variety of complications, especially during the early post-transplant period. Radionuclide scintiphotography has been found to be a valuable method for evaluation of renal transplant function and for detection of some of the more frequent complications (2,3,4,5). Because of this, scintiphotography now has a major role in transplant evaluation. This paper will review the radionuclide procedures available and their current use in evaluation of renal transplants.

Scintigraphic Procedures. The transplanted kidney is routinely placed in the iliac fossa. This location allows the kidney, ureter, and bladder to be included in the field of view of a standard scintillation camera. The procedures currently in use are:

1. kidney and bladder scintigraphy using ^{131}I-orthoiodohippurate.
2. scintigraphy of blood flow distribution followed by kidney and bladder imaging using ^{99m}Tc-Sn-DTPA.
3. scintigraphy using ^{99m}Tc-sulfur colloid.
4. scintigraphy combined with transplant renogram or other function studies.

Iodine-131-hippurate scintigraphy. Scintiphotographs of the kidney and bladder area are obtained approximately every 4 minutes for 20 to 30 minutes. If the bladder is filled, the patient then voids or the catheter is unclamped and a post-voiding picture is obtained. In a normal study there should be uniform maximum concentration in the renal parenchyma at 4 minutes with excretion into the bladder at 8 minutes and decreasing renal concentration by 20 minutes. Figure 1 shows an example of a normal study.

Perfusion sequence and scintigraphy with ^{99m}Tc-Sn-DTPA. This tracer is excreted exclusively by glomerular filtration and is not as rapidly cleared from plasma as is hippurate. Sufficient radioactivity can be given to visualize the major vessels and renal perfusion if rapid sequential scintiphotos are obtained immediately after a bolus injection. A normal study of this type is seen in Figure 2. If renal function is good, there will be rapid excretion of the tracer and subsequent scintiphotos will show the kidney and urinary tract as seen in Figure 3. If renal function is moderately impaired, however, excretion becomes markedly delayed and may not be adequate for visualization. Hippurate may still give adequate visualization in this case, so that hippurate remains the most dependable tracer for routine use, even though Tc-Sn-DTPA may in some cases give better visualization.

Scintigraphy with ^{99m}Tc-sulfur colloid. Colloidal tracers are not normally concentrated in the kidney. However, when the changes of chronic rejection develop, colloidal tracers are localized to some extent

Presented by Dr. Haden at the Postgraduate Course in Nuclear Medicine, February 27, 1975, in Williamsburg, Virginia.

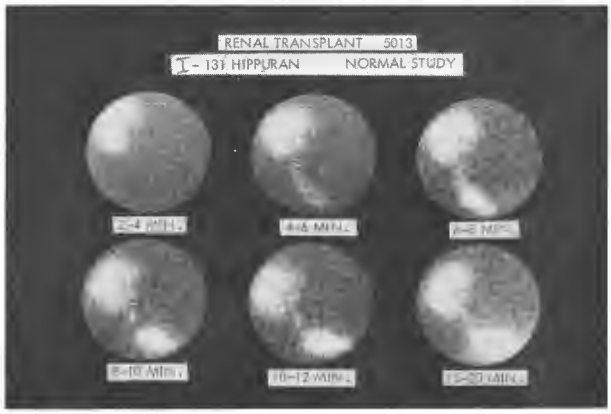

Fig 1—Normal scintiphotographic transplant study using ^{131}I-hippurate. Kidney is seen in first picture and ureter and bladder are visualized in later pictures. Time periods are indicated.

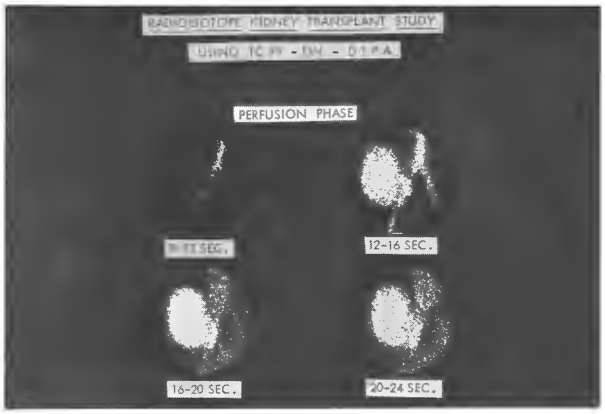

Fig 2—Scintiphotos from a transplant perfusion study using ^{99m}Tc-Sn-DTPA. Terminal aorta, iliac arteries, and transplanted kidney are seen.

in the kidney and can be demonstrated on scintiphotography. One technique is to use a diverging collimator so as to include the bony pelvis but exclude the liver image (6). The concentration in the kidney is then compared with that in the bones. An example of this study in two separate patients is shown in Figure 4. Both patients had mild to moderate chronic rejection but well-preserved renal function. We have not found this study to be very useful since it does not dependably detect acute rejection and almost all of the transplants eventually develop some degree of chronic rejection.

Scintigraphy combined with renogram or other function studies. Scintigraphy with ^{131}I-hippurate provides only a crude and semiquantitative measure of renal function. A transplant renogram can be obtained simultaneously and gives an additional method of comparing serial studies but is cumbersome to obtain with standard equipment. If the intravenous dose is precisely measured and subsequent blood and urine collection are made, the effective renal plasma flow may be calculated. The value of these additional measurements is not established and they are not routinely used.

Disorders of Transplant Function. The main criterion for satisfactory transplant function is an adequate urine output. Serious complications are usually manifested by a decrease in urine output.

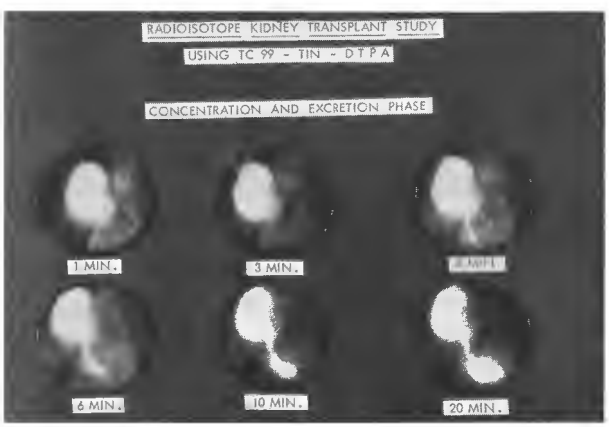

Fig 3—Normal scintigraphic transplant study of excretion phase using ^{99m}Tc-Sn-DTPA. Kidney, ureter, and bladder are clearly seen.

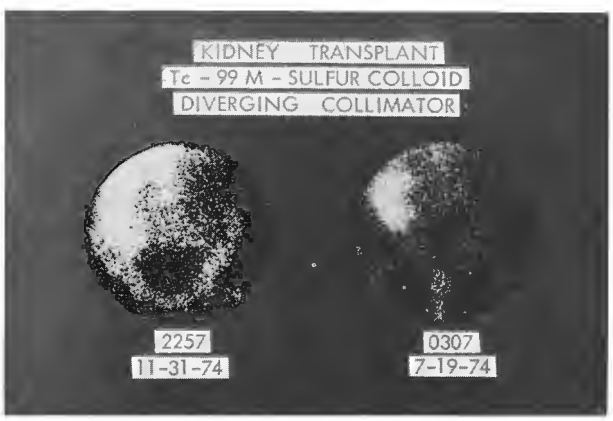

Fig 4—Scintiphotographs of transplanted kidney after I.V. injection of ^{99m}Tc-sulfur colloid. Two separate patients. On the left, concentration is seen in the lumbar spine, pelvis, and in the kidney in the right iliac fossa. On the right, the kidney concentration is so much greater than the bones that pelvis, spine, and upper femur are only very faintly seen.

Table 1 gives a list of the common causes of acute oliguria in transplant recipients. When oliguria occurs, the cause must be promptly determined as a guide to effective treatment.

Acute tubular necrosis is the most common cause of acute oliguria following soon after transplantation, especially with cadaver transplants, and is completely reversible with adequate treatment. If associated with the transplant procedure, this complication occurs within the first 48 hours after surgery. Acute rejection, obstructing clots, and ureteral leaks are also common. Arterial and venous occlusion are uncommon, and we have not yet had cortical necrosis occur. Lymphocele is a collection of lymph adjacent to the transplanted kidney which may occur following interruption of lymphatics in that area. Lymphoceles usually cause compression or displacement of the ureter and bladder and may produce urinary obstruction. They do not occur until after the first week and may not develop until six to eight months after transplantation.

Diagnostic Studies for Acute Oliguria. The various causes of oliguria listed in Table 1 cannot be differentiated on a clinical basis. Prompt diagnosis is obviously of critical importance since the treatment for each cause is different and may entail additional risk. The order of diagnostic studies used by M. J. V. Smith, MD, of the Medical College of Virginia Urology Division is given in Table 2 (7) (oral communication, February, 1975).

The first item on this list, the one-hour biopsy, refers to a kidney biopsy obtained at the end of the transplant procedure. This may show early evidence of acute rejection. The first four steps on this list are without risk and often give sufficient diagnostic information to determine treatment. The subsequent procedures should be performed only if necessary because of added risk, especially since these patients all receive aggressive immunosuppressive therapy.

TABLE 1
Causes of Acute Oliguria in Renal Transplant

Vascular
Arterial thrombosis
Venous thrombosis
Parenchymal
Acute tubular necrosis
Acute rejection
Cortical necrosis
Ureter
Clots
Leaks
Edema at anastomosis
Necrosis and retraction
Bladder
Leaks or perforations
General
Lymphocele

TABLE 2
Acute Oliguria in Renal Transplant
Order of Diagnostic Studies

1. one-hour biopsy
2. irrigate catheter
3. KUB x-ray
4. scintigram
5. cystogram
6. cystoscopy
   a. bulb retrograde
   b. catheter retrograde
7. arteriography

Scintigraphic Findings in Transplant Disorders. A brief tabulation of the scintigraphic findings in transplant disorders is given in Table 3.

Acute tubular necrosis. With acute tubular necrosis the kidney will still concentrate hippurate in the renal parenchyma, although the concentration is somewhat decreased and maximum concentration is delayed. Typically, no excretion into renal pelvis or

TABLE 3
Scintiphotography of Renal Transplants
Using ^{131}I-Orthoiodohippurate

Normal
Uniform maximum concentration in renal parenchyma at 4 minutes
Excretion into bladder by 8 minutes
Decreasing renal concentration by 20 minutes
Acute Tubular Necrosis
Delayed concentration
No excretion
Acute Rejection
Delayed concentration
Irregular concentration
Delayed excretion
Acute Tubular Necrosis with Added Rejection
Delayed irregular concentration compared with baseline
Ureteral Obstruction
Retention of tracer proximal to obstruction
Ureteral Leak
Tracer outside urinary tract
Vascular Occlusion—Arterial
No activity in kidney

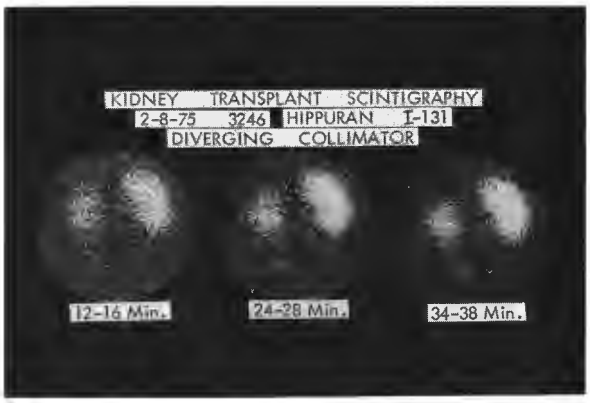

Fig 5—Selected scintigraphs obtained in a patient with two transplanted kidneys studied with ^{131}I-hippurate. Both kidneys are seen. The kidney on the patient's right (observer's left) was transplanted 15 months previously and is the site of severe chronic rejection. The other kidney was inserted one day previously and is not functioning because of acute tubular necrosis.

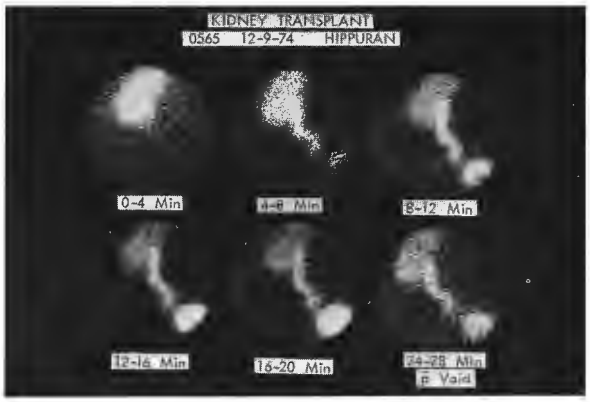

Fig 6—Transplant scintigraphic study four days post-transplant with good function.

bladder is visualized. Figure 5 shows pictures selected from a series of scintigraphs obtained because of severe oliguria one day after transplantation of a second kidney into the left iliac fossa. The first kidney was inserted 15 months previously on the right side and had developed severe chronic rejection. The rejected kidney is visualized on the patient's right (observer's left) as an area of poor concentration suggesting a small kidney. The new transplant is well visualized on the patient's left (observer's right), but maximum concentration is definitely delayed and no excretion from the kidney is seen even after 30 minutes. Within a week there was good function of the new kidney.

Rejection. Rejection may be of varying acuteness and severity. Hyperacute rejection occurs immediately after transplantation and is associated with severe acute inflammatory and vascular changes in the kidney. Thrombosis of small vessels occurs, and on scintigraphic study the findings may be the same as in arterial occlusion. The transplanted kidney must always be removed following hyperacute rejection. Rejection of less severity may occur at any time following transplantation. This reaction may develop quite abruptly and may cause sudden oliguria. On scintigraphic study, acute rejection produces delayed and sometimes irregular concentration of hippurate. Excretion is also delayed or may be absent. Figures 6 and 7 show scintigraphic studies of a patient who received a transplant on 5 December, 1974. The scintigraphic study on 9 December, 1974, (Fig 6) shows that the kidney is working quite well. On 11 December, 1974, the patient developed sudden oliguria, and a repeat study on that day is shown in Figure 7. Concentration is delayed and there is no excretion. These findings are compatible with either acute tubular necrosis or acute rejection. However, the time after transplantation and the demonstration of good function two days previously exclude acute tubular necrosis resulting from the transplant procedure as a cause of the acute oliguria. This patient was treated for acute rejection with resulting improvement.

Chronic rejection is associated with delayed concentration and delayed excretion as shown in Figure 8. These findings are not specific for chronic rejection since they may occur with other chronic parenchymal disease of the kidney. Concentration of colloidal par-

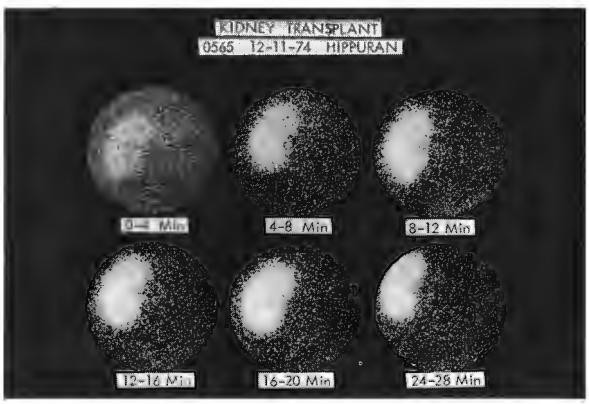

Fig 7—Same patient as Fig. 6 two days later. Acute rejection.

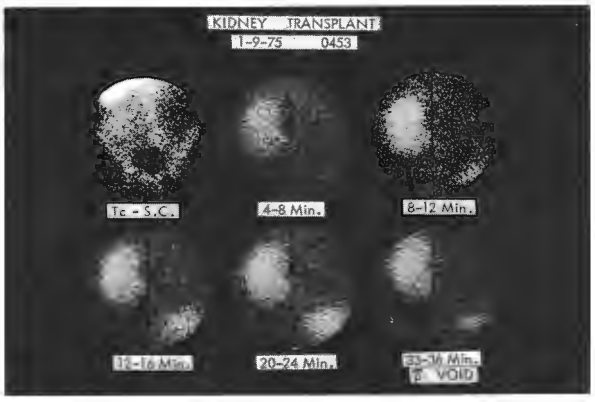

Fig 8—Sulfur colloid and hippurate scintigraphs in chronic rejection.

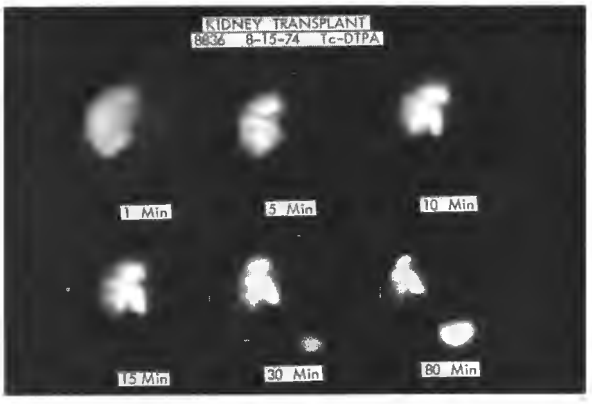

Fig 9—Partial ureteral obstruction producing retention in pelvis and upper ureter, delayed visualization of bladder.

ticles can be demonstrated in chronic rejection, but this has not been particularly helpful since essentially all of the transplants develop some degree of chronic rejection.

Rejection may be of varying degree and may occur in combination with acute tubular necrosis or other disorders. This may be quite difficult to detect. However, any deterioration of renal function on scintigraphic study after the first 24 hours usually indicates rejection. It is, therefore, good practice to obtain an initial scintigraphic study at 24 to 48 hours after transplantation as a baseline for subsequent studies. Changes due to acute tubular necrosis will be maximal at 24 hours.

Ureteral obstruction. The ureter may be obstructed early by clots or later by stones or by compressing lesions such as lymphoceles. As long as renal parenchymal function remains good there will be good concentration of hippurate by the kidney. Scintigraphic study shows accumulation of tracer proximal to the obstruction with delayed or absent excretion into the bladder. An example of partial obstruction of the upper ureter is shown in Figure 9.

Ureteral leaks. Extravasation of urine from the ureter or from the ureterovesical junction is a common and serious complication of renal transplantation. It has occurred in 8% to 30% of several series with a mortality rate of 25% to 50%. Ureteral leak is readily demonstrable by scintigraphic study, but one must be careful to follow the study long enough to fully evaluate any unusual appearance. It is also wise to obtain post-voiding films to clearly establish bladder location. Figure 10 shows several pictures from a study obtained one month after transplantation. The patient had increasing serum creatinine, but no local signs and was thought to have mild rejection. An abnormal collection is seen adjacent to the bladder in the early pictures, and at 25 minutes there is a wide area of abnormal concentration extending along the path of the ureter. The picture at two hours shows the radioactivity located in extravasated urine collected around the bladder, ureter, and lower pole of the kidney. The 10-minute picture also shows some retention of tracer in the renal pelvis and collecting system suggesting mild partial obstruction associated with the urinoma.

Vascular occlusion. With arterial occlusion the kidney is not perfused and no tracer is concentrated in the kidney. Using ^{99m}Tc-pertechnetate or DTPA, the major vessels can be visualized and the lack of perfusion can be demonstrated as shown in the top

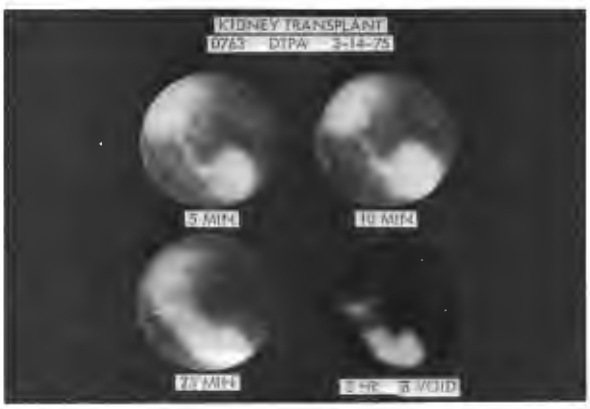

Fig 10—Progressive urine extravasation from ureterovesical junction.

half of Figure 11. When hippurate is the tracer, scintiphotos over the kidney simply show no concentration in the renal parenchyma as at the bottom of Figure 11. These findings may occur in primary arterial occlusion or in hyperacute rejection with thrombosis of small vessels. In either case, surgery is required for removal of the kidney unless a vascular occlusion can be repaired. Venous occlusion, if complete, will block vascular perfusion and is usually followed by thrombosis in the arterial supply. However, venous thrombosis may partially block vascular flow and the kidney may survive after a period of decreased function. If there is viable and perfused renal tissue still present then there should be some concentration of hippurate. It is generally felt, though not completely proven, that the absence of any demonstrable concentration of hippurate indicates that the kidney is no longer viable and should be removed.

Management of Transplant Oliguria Based on Scintigraphic Findings. When oliguria develops in the transplant recipient, the results of the scintigraphic study together with clinical findings will usually indicate the management to be followed. This is briefly summarized in Table 4. If the oliguria develops within the first 48 hours and the scintigram shows a clear renal image with decreased excretion, management for acute tubular necrosis is indicated. If the time period is not compatible with acute tubular necrosis or if subsequent scintigrams show further deterioration, then rejection has developed. If there is no renal image with hippurate or technetium, then surgery is required. An arteriogram can be done if it is necessary to differentiate between hyperacute rejection and arterial occlusion. Ureteral obstruction will usually be evident on the scintigraph, but further diagnostic procedures will be required to determine the cause. Extravasation will also be evident on the scintigraph, but further studies will be required to localize the precise site and extent. In some cases, extravasation can be treated without surgery if infection does not develop.

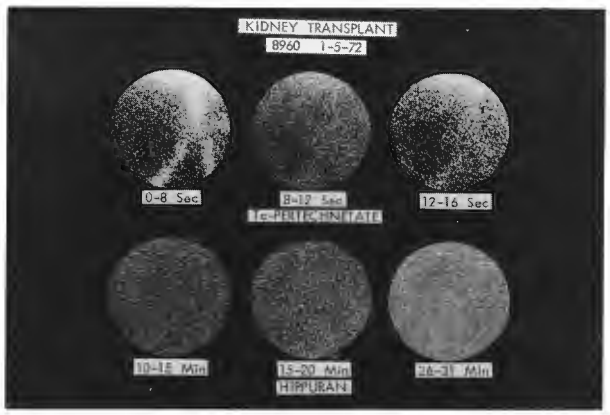

Fig 11—Arterial occlusion. Upper pictures with ^{99m}Tc-pertechnetate show terminal aorta and iliac arteries with "cold" area over kidney. Lower pictures made with ^{131}I-hippurate show no concentration in kidney.

TABLE 4
Hippurate Scintiphotography in Management of Acute Oliguria in Renal Transplants

1. Clear renal image with decreased excretion:
   Conservative Management
   A. If image deteriorates on subsequent study:
   Treat Rejection
2. No renal image:
   Study with Pertechnetate Bolus
   A. If no perfusion:
   Arteriogram or Surgery
3. Ureteral obstruction:
   Retrograde or I.V. Urogram or Surgery
4. Extravasation:
   Retrograde Urogram or Surgery

Conclusions.

1. Scintiphotography of the kidney and bladder using ^{131}I-hippurate is the basic procedure for transplant evaluation. This is a dependable method for determining transplant viability and function. It is also a dependable method for detecting ureteral leak or obstruction, provided that renal function is adequate.
2. Concentration of hippurate indicates that the kidney has a blood supply, is viable, and has recoverable function. Absence of hippurate concentration indicates severe and probably irreversible kidney damage.
3. Scintiphotography with ^{99m}Tc-Sn-DTPA gives good resolution in normally functioning kidneys. With severely impaired renal function, this tracer is inferior to ^{131}I-hippurate.
4. Rapid sequence scintigraphy of the initial circulation using technetium tracers can visualize major vessels and renal perfusion. Quantitation and comparison between studies are difficult.
5. A single scintiphotographic study will not differentiate between acute tubular necrosis and rejection. Serial scintiphotographic

studies may indicate rejection if deterioration of function is shown to occur later than 24 hours after transplantation.

6. Colloidal tracers may concentrate in the kidney in chronic rejection. This phenomenon has not yet been clinically helpful.
7. The scintigraphic findings in transplant disorders have been reviewed and a schema for management based on these findings has been presented.

Figures 1 and 3 are reprinted from the *Journal of Nuclear Medicine,* Vol. 16, No. 7, with permission of publisher.

REFERENCES

1. The 11th report of the Human Renal Transplant Registry, ADVISORY COMMITTEE TO THE RENAL TRANSPLANT REGISTRY. *JAMA* 226:1197-1204, 1973.

2. SALVATIERRA O JR, POWELL MR, PRICE DC, ET AL: the advantages of ^{131}i-orthoiodohippurate scintiphotography in the management of patients after renal transplantation. *Ann Surg* 180:336-342, 1974.

3. WEISS ER, BLAHD WH, WINSTON MA, ET AL: Scintillation camera in the evaluation of renal transplants. *J Nucl Med* 11: 69-77, 1970.

4. STAAB EV, WHITTIER F, PATTON DD, ET AL: Early evaluation of cadaver renal allotransplant by means of radionuclide imaging. *Radiology* 106:147-151, 1973.

5. ROSENTHALL L, MANGEL R, LISBONA R, ET AL: Diagnostic applications of radiopertechnetate and radiohippurate imaging in post-renal transplant complications. *Radiology* 111:347-358, 1974.

6. GEORGE EA, CODD JE, NEWTON WT, ET AL: Visualization of rejecting renal transplants with ^{99m}tc sulfur colloid (tsc), abstracted. *J Nucl Med* 15:493, 1974.

7. SMITH MJV: Anuria in the recipient, in Hume DH, Rapaport FT (eds): *Clinical Transplantation,* New York, Grune & Stratton, 1973, p. 225-227.