2.1 Introduction

Scintigraphy has provided a unique tool for the noninvasive evaluation of renal pathophysiology, and there is still a rapid increase in the scope and number of radionuclide renal studies. This chapter familiarizes the reader with the most frequently used procedures encountered in nuclear medicine in genitourinary system. These include studies for renovascular hypertension, urinary tract obstruction, urinary tract infection, renal transplant complications, and testicular torsion.

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2.2 Radiopharmaceuticals

Several radiotracers are used for imaging genitourinary system conditions. These include renal radiopharmaceuticals for dynamic and static studies, Tc99m sulfur colloid for direct vesico-ureteral reflux study and Tc99m-pertechnetate for scrotal imaging.

Renal radiopharmaceuticals can be described in two broad classes — those that are excreted rapidly into the urine and those that are retained for prolonged periods in the renal parenchyma.

1. Rapidly excreted radiopharmaceuticals are used in dynamic imaging studies to assess individual renal function and include the following:
   (a) $^{99m}$Tc-mercaptoacetyltriglycine (MAG3) which is the agent of choice, is 90% protein bound, and excreted almost exclusively by the renal tubules. High renal-to-background count ratios provide excellent images and permit visualization of poorly functioning kidneys.
   (b) $^{99m}$Tc-diethylenetriamine penta-acetic acid (DTPA) which was the most popular radiopharmaceutical in its category prior to the introduction of $^{99m}$Tc-MAG3. It shows little protein binding (about 5%) and is excreted exclusively by glomerular filtration. Renal uptake of $^{99m}$Tc-DTPA is limited because only 20% of the renal blood flow is filtered by the glomeruli. The 20% extraction fraction is considerably lower than that of $^{99m}$Tc-MAG3 and yields lower renal-to-background uptake ratios. However it is less costly and may be used as an alternative to $^{99m}$Tc-MAG3, particularly if a quantitative estimate of GFR is also needed.

2. The slowly excreted radiopharmaceuticals include $^{99m}$Tc-dimercaptosuccinic acid (DMSA) and $^{99m}$Tc-glucoheptonate. Prolonged cortical retention of these radiopharmaceuticals allows the assessment of parenchymal morphology, and since accumulation occurs only in functioning tubules, uptake can be quantified to assess accurately the differential renal function. The preferred agent, Technetium-99 m-DMSA, is 90% protein bound and accumulates in functioning tubules. Since very little of the radiotracer is excreted, interference from collecting system activity, particularly on delayed images, is minimal. A total of about 40% of the administered amount is accumulated in the renal cortex.

2.3 Imaging Studies

(a) Renal scintigraphy

According to the types of renal radiopharmaceuticals, renal scintigraphy can be of dynamic or static nature.

- Dynamic studies are obtained using the rapidly excreted radiopharmaceuticals. Dynamic studies start by rapid acquisition of image frames upon injection of the
tracer to follow activity while passing through the blood vessels till reaching the kidneys to evaluate the blood flow (Fig. 2.1a). This phase is followed by another series of imaging frames every 10–20 s of the kidney to evaluate the kidney functional handling of the radiotracer (Fig. 2.1b). This phase will then be computer processed to generate time–activity curve (renogram) for both kidneys to illustrate the uptake, build up, and excretion of the radiopharmaceutical by each kidney (Fig. 2.1c) and generate the percent contribution of each kidney to the total renal function (split or differential renal function).

Static studies using slowly secreted radiopharmaceuticals, particularly Tc99m DMSA, are acquired 3 h after intravenous injection of the radiotracer and optionally up to 24 h based on the individual case and the kidney function. Anterior, posterior, left, and right posterior oblique views are obtained. These studies are predominantly used to accurately determine the split renal function and in cases of urinary tract infections to evaluate the changes including cortical scars: Using the anterior and posterior views the split renal function is calculated by the geometric mean of the background subtracted kidney counts.

(b) Vesicoureteral reflux study
(c) Scrotal imaging study
2.4
Clinical Uses

2.4.1
Dynamic Renal Scintigraphy

- Evaluation of renal perfusion and function
- Diagnosis of renovascular hypertension
- Diagnosis and follow-up of urinary tract obstruction
- Evaluation of renal transplant complications

2.4.2
Static Renal Scintigraphy

- Urinary tract infections
- Evaluation of renal masses
- Quantitating differential renal function
- Congenital renal malformations (horseshoe kidney)

2.4.3
Vesicoureteral Reflux Study

Diagnosis and follow-up of vesicoureteral reflux

2.4.4
Scrotal Imaging

Diagnosis of testicular torsion and inflammation

2.5
Commonly Used Applications

2.5.1
Diagnosis of Renovascular Hypertension

The role of the renin-angiotensin system, i.e., maintenance of systemic blood pressure, is well played in such conditions as hypotension and shock. In significant renal artery stenosis, however, activation of the renin-angiotensin system is a mixed blessing, limiting a fall in GFR but causing systemic (renovascular) hypertension. Systemic blood pressure is
maintained primarily by increase in vascular tone and retention of sodium and water, while a sharp reduction in GFR is prevented by increase in the glomerular capillary hydrostatic pressure.

Glomerular capillary hydrostatic pressure is modulated by the tone of the afferent and efferent glomerular arterioles. Increased tone in the efferent arteriole or decreased tone (increased flow) in the afferent arteriole raises capillary hydrostatic pressure and GFR, while decreased tone in the efferent arteriole or increased tone (decreased flow) in the afferent arteriole lowers GFR.

The scintigraphic diagnosis of renovascular hypertension is based on the demonstration of changes in renal physiology following the administration of an ACE inhibitor. Angiotensin II, formed by the activation of the renin-angiotensin system, helps maintain GFR by increasing the tone of the efferent glomerular arteriole which, in turn, raises the glomerular capillary hydrostatic pressure. These changes are reversed by ACE inhibitors, which block the conversion of angiotensin I to angiotensin II. Consequently, there is a sharp drop in GFR and in proximal tubular urine flow.

Decreased GFR and tubular flow after the administration of an ACE inhibitor will result in decreased uptake and prolonged cortical retention of $^{99m}$Tc-DTPA, which is excreted by glomerular filtration. On the other hand, $^{99m}$Tc-MAG3, which is a tubular and blood flow agent, shows only prolonged cortical retention without apparent decreased uptake since renal blood flow generally is not significantly changed (Figs. 2.2 and 2.3). Rarely, uptake of $^{99m}$Tc-MAG3 may actually decrease, presumably due to a fall in blood pressure below a critical level required to maintain perfusion in the stenotic kidney.

![Time activity curve (renogram)](image)

**Fig. 2.2** Normal captopril study with normal excretion and no cortical retention of activity bilaterally (arrows)
2.5.2 Urinary Tract Obstruction

The most commonly used radiotracer for diuretic renography is Tc99m mercaptoacetyltriglycine (MAG-3).

Urinary tract obstruction may be high grade complete or partial, and it may occur at various locations including the ureteropelvic junction (UPJ), ureterovesical junction (UVJ), and bladder outlet. The clinical consequences are quite dramatic and predictable in an acute and complete obstruction, but not in a partial and chronic one, exemplified by UPJ obstruction in children. Chronic UPJ obstruction may eventually lead to renal cortical atrophy.

Diuretic renography is based on the premise that increased urine flow resulting after furosemide administration causes rapid “washout” of radiotracer from the unobstructed collecting system (Fig. 2.4), but delayed washout if obstruction is present (Figs. 2.5 and 2.6). The washout half-time following diuretic injection is determined from the time-activity curve. A half time of 10 min or less is considered normal, 10–20 min equivocal, and more...

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**Fig. 2.3** Abnormal captopril study showing retention of activity in right kidney with Captopril on time–activity curve (arrow) compared to the baseline study (lower curve) where there is good clearance (arrow)
than 20 min abnormal. Given the dynamic nature of UPJ obstruction, however, a number of factors may influence the diuretic renogram and must be taken into consideration for a proper assessment.

2.5.3 Urinary Tract Infection

Pyelonephritis refers to infection of the renal tubules, pelvis, and interstitium, and it has a wide spectrum of clinical presentations. While the clinical diagnosis is obvious when characteristic manifestations of flank or back pain, fever, and bacteriuria are present, pyelonephritis may be missed if symptoms are absent or referable only to the lower urinary tract. Acute pyelonephritis requires more vigorous treatment than lower urinary tract infection, and, left untreated, it can lead to scarring and renal insufficiency. Consequently, identification of renal involvement is critical in children with suspected urinary tract infection, and parenchymal scintigraphy with the tubular agent, Tc-99 m-dimercaptosuccinic acid (DMSA) can play an important role in their diagnostic evaluation.
Ascending infection from the lower urinary tract is the usual mechanism for pyelonephritis. The infection appears to originate in the urethra or the vaginal introitus, which are colonized by enteric flora, predominantly *Escherichia coli*, and it is more common in females, presumably due to their shorter urethra. Structural abnormalities of the urinary tract such as vesicoureteral reflux and bladder outlet obstruction (which exacerbate reflux) are important predisposing factors, though often not demonstrable. Another predisposing factor appears to be an inborn increase in uroepithelial cell susceptibility to bacterial adherence, which facilitates bacterial ascent to the upper urinary tract. Finally, catheterization and sexual intercourse can allow urethral bacteria to enter the bladder. Ascending infection eventually reaches the renal calyces, from which microorganisms enter the parenchyma through the papillae by intrarenal reflux.

Fig. 2.5 Left-sided urine outflow obstruction in a 4-year-old patient with left hydronephrosis before (a) and after lasix injection (b). The preoperative study shows decreased uptake in the left kidney and slow accumulation of the radiotracer. After lasix injection there is retained activity in the left kidney due to poor response compared to right kidney which shows good uptake and complete clearance. The study was repeated after surgery and there is better uptake and accumulation of activity before lasix injection (c) and clearance of activity from the left kidney after lasix injection (d)
Scarring of the renal parenchyma may result from pyelonephritis. It is a common cause of hypertension and, if sufficiently extensive, it can lead to progressive renal insufficiency and end-stage renal disease. Although vesicoureteral reflux is frequently associated with scarring, it is not a prerequisite for this condition.

Imaging of the renal parenchyma with $^{99m}$Tc-DMSA offers a simple and accurate method for detecting acute pyelonephritis in the child with urinary tract infection. $^{99m}$Tc-DMSA localizes in functioning proximal tubular cells and is not excreted in significant amounts, so that imaging at 4–24 h after radiopharmaceutical administration reveals primarily cortical uptake without interfering activity in the collecting system (Fig. 2.7).
A cortical defect due to pyelonephritis is characterized by preservation of renal contour, whereas scarring (from a previous infection) typically results in volume contraction, although the two may be indistinguishable (Figs. 2.8 and 2.9). Such distinction may become less relevant as scarring declines with the routine use of $^{99m}$Tc-DMSA imaging in children with urinary infection.

In addition to imaging during the acute phase of the disease, follow-up studies are done to confirm resolution of the pyelonephritic defect(s) and absence of cortical scarring. Patients with scars are followed periodically with imaging and measurement of relative function for assessment of progressive renal insufficiency.

Magnetic resonance imaging (MRI) and spiral CT are other modalities that may be helpful in the evaluation of pyelonephritis.

Fig. 2.8 Tc99m DMSA study of a 4-year-old female child with UTI. Study shows defect in the right upper pole (arrow)
2.5 Commonly Used Applications

2.5.4 Vesicoureteral Reflux

Urinary tract infection is a common problem in children. Approximately 40% of patients with upper urinary tract infection have vesicoureteral reflux. Misdiagnosed or inadequately treated urinary tract infection can lead to serious complications such as hypertension and chronic renal failure.

Direct radionuclide cystography using Tc99m Sulfur colloid is a method to evaluate for vesicoureteral reflux, which has several advantages including significantly less gonadal radiation when compared with conventional radiographic technique, voiding cystourethrogram (VCUG). The international radiologic grading includes 5 grades using some detailed anatomy such as characterization of the fornices that is impossible to achieve by scintigraphic studies. Accordingly a more simplified scintigraphic grading attempt classifies reflux into 3 grades (Table 2.1 and Fig. 2.10) Mild (I), Moderate (II) and Severe (III).

The test is recognized for the initial evaluation of females with urinary tract infection for reflux, diagnosis of familial reflux, and for the evaluation of vesicoureteral reflux after medical and/or surgical management (Fig. 2.11).

Table 2.1 Scintigraphic grading for vesicoureteral reflux

<table>
<thead>
<tr>
<th>Grade</th>
<th>Reflux Description</th>
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<tbody>
<tr>
<td>Mild (Grade I)</td>
<td>Reflux into ureter</td>
</tr>
<tr>
<td>Moderate (Grade II)</td>
<td>Reflux into pelvocalyceal system</td>
</tr>
<tr>
<td>Severe (Grade III)</td>
<td>Reflux into pelvocalyceal system with dilated pelvis or both pelvis and ureter</td>
</tr>
</tbody>
</table>
Fig. 2.10 Grades of vesico-ureteral reflux used for radionuclide studies

Fig. 2.11 (a) Vesicoureteral reflux study showing right side grade II reflux (arrow). (b) Bilateral vesicoureteral grade III reflux
2.5.5 Evaluation of Renal Transplant Complications

Advances in our understanding of the pathophysiology of renal transplants over the past several years have resulted in significant improvement in renal graft survival and an increase in the number of transplantations. The key factors influencing survival are donor–recipient histocompatibility and donor status (living related, living unrelated, or cadaver). Graft survival is best when the donor is an HLA-identical sibling, and better for living-related than for cadaver donors with similar HLA matches. A host of other factors, including harvesting and transplantation technique, cold ischemia time (between harvest and transplantation), donor/recipient age, recurrence of primary renal disease, and race also play an important role in graft survival. Renal scintigraphy helps evaluate the perfusion and function of transplanted kidney (Fig. 2.12) and detect and follow

Fig. 2.12 Normal perfusion (a) and function (b) of a transplanted kidney with representative images with labeled diagrams illustrating the structures on images
postoperative complications. The surgical and medical complications of renal transplantation are considered below.

2.5.5.1 Surgical Complications

Scintigraphic studies can be used effectively to evaluate urine extravasation (Fig. 2.13), ureteral obstruction, hematoma, lymphocele, and renal artery stenosis.

2.5.5.2 Medical Complications

Acute Tubular Necrosis

Acute tubular necrosis (ATN), characterized by ischemic necrosis of the tubular epithelial cells and decreased GFR, is frequently associated with cadaver renal transplants. Possible causes are hypotension/hypovolemia in the donor and prolonged interval between harvest and transplantation. After transplantation, urine output usually starts to decrease within the first 24 h or so and improves spontaneously after a few days, although ATN may occasionally last a few weeks. It is often difficult to make a clinical distinction between ATN and rejection in the post-transplantation period. A clear scintigraphic distinction between these two conditions also has remained elusive, for two reasons. First, the scintigraphic diagnosis of ATN rests on the premise that graft perfusion is preserved despite decreasing function, in contrast to rejection, where both perfusion and function decrease. However, depending on the severity/stage of ATN, graft perfusion may vary. Second, ATN and acute rejection may coexist. Recovery of the condition can best be ascertained by serial scintigraphy.

Fig. 2.13  Tc 99m MAG-3 study obtained for a patient after renal transplantation. There is extravasation of activity indicating postoperative leak (arrow)
2.5 Commonly Used Applications

Rejection

According to Banff Classification rejection can be of the following types:

1. Antibody-mediated rejection: Two types of antibody-mediated rejection are described, immediate or hyperacute, and delayed or accelerated acute. Hyperacute rejection is caused by preformed antidonor antibodies. Rejection may begin within minutes or hours and is usually apparent during surgery. Scintigraphy shows a photopenic region corresponding to the avascular graft. Fortunately, hyperacute rejection is rare and largely preventable by appropriate screening tests.

   Accelerated acute rejection may be considered a “slow” variant of hyperacute rejection, mediated primarily by antidonor antibodies. It usually occurs on the second or third day following transplantation, after allograft function has been established. Scintigraphy generally shows poor radiotracer uptake in the graft.

2. Acute/active rejection: Acute rejection is the most frequent type of rejection confronting the nuclear medicine physician (Fig. 2.14). It is most common in the first 4 weeks following transplantation but may occur at any time between 3 days and 10 or more years.

3. Chronic/sclerosing allograft nephropathy: Chronic/sclerosing nephropathy generally occurs 6 months to years after transplantation. It may be related to a number of causes including chronic rejection, hypertension, an infectious/noninfectious inflammatory process, and effects of medications.

2.5.6 Diagnosis of Testicular Torsion

Testicular torsion is an emergency condition which needs immediate diagnosis and management. In most institutions, Doppler ultrasound is used most commonly as the

![Fig. 2.14 Tc 99 m MAG-3 study for a patient with renal transplantation showing decreased perfusion (a) and function (b) of the graft illustrating the typical scintigraphic findings of rejection](attachment:image.png)
standard imaging technique of choice to confirm the diagnosis in most cases. Scintigraphy is used when color Doppler is inadequate, raising doubts about the suspected torsion. Recent studies, however, comparing both modalities indicate that scintigraphy is more accurate for the diagnosis of testicular torsion. The study is performed using Tc99m-pertechnetate injected IV and show normally symmetrical and uniform perfusion (Fig. 2.15). In acute torsion, there is decreased perfusion to the affected side (Fig. 2.16) while in epididymitis which may be clinically difficult to differentiate from

**Fig. 2.15** Normal scrotal imaging study obtained using Tc99m pertechnetate

**Fig. 2.16** Scrotal imaging study illustrating left side acute torsion indicated by decreased uptake (arrow)
torsion the study shows increased perfusion (Fig. 2.17). Torsion of long duration (missed torsion) appears as an area of decreased perfusion surrounded by a rim of increased uptake (Fig. 2.18).

Fig. 2.17 Scrotal imaging study showing increased activity in the left side (arrow) in a case of epididymitis

Fig. 2.18 Scrotal imaging study demonstrating the pattern of torsion of long duration in the left side (arrow) with markers around the affected testicle (right side)
2.6 Summary

Radionuclide imaging plays a very important role in genitourinary diseases. It is instrumental in the diagnosis and follow-ups of urine outflow obstruction in adults and more importantly in pediatric age group. It also plays an important role in detecting complications of urinary tract infection and is part of the management protocols. It also helps in the detection and more importantly follow-up of vesicoureteral reflux and evaluation of renal transplantation and its complications. It helps differentiate testicular torsion from epididymitis/epididymo-orchitis and other conditions.

Further Reading

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