# Chapter 31

# KIDNEYS AND URINARY SYSTEM

Gopinathan Nair

## Anatomy and physiology

Nuclear medicine studies, though primarily concerned with the functional aspects of the organ, can also provide useful information about the anatomy. An understanding of the anatomy and physiology of the kidneys and urinary system greatly helps in the interpretation of data from radionuclide studies.

The various anatomical regions are shown in (**Fig. 31.1**). The outermost region, the renal cortex, contains most of the glomeruli and the proximal convoluted tubules. The inner region, the renal medulla contains all the collecting tubules which open into the renal papillae. Urine flows from the ducts in the papillary tips into a minor calyx. Minor calyces unite to form a superior and inferior major calyx which join to form the renal pelvis. The pelvis is continuous with the ureter. In a good renal scintigraphic image, it will be possible to identify the cortex and medulla - essentially the urine-forming and urine-draining system - and draw regions of interest to separate these functionally different compartments. The renal hilus marks the region where the major renal vessels enter or leave the kidney.

The ureters enter the bladder through the orifices situated at the two corners of the triangle called the trigone. The ureters pierce the muscle and mucosal walls obliquely. This arrangement helps in the prevention of reflux of urine as the intravesical pressure increases. As the bladder contracts, the urine leaves through the orifice into the urethra.

The functional unit of the kidney is the nephron. There are approximately 100 000 nephrons in each kidney. A nephron is composed of a glomerulus, and in succession, a number of tubular segments. Collecting tubules from several nephrons progressively unite to form collecting ducts which join other collecting ducts and ultimately empty their contents into a minor calyx through the duct in the papillae.

The glomerulus is composed of a plexus of capillaries and a covering of epithelial cells. Glomerular capillaries arise from the afferent arteriole and reunite to form the efferent arteriole. The capillaries are covered on their external surface by a thin layer of epithelial cells, the visceral layer of Bowman's capsule. This layer of Bowman's capsule is continuous with the epithelium of the proximal convoluted tubule via the parietal layer of Bowman's capsule. The Bowman's space is continuous with the lumen of the proximal convoluted tubule. The process of urine formation begins with the filtration of plasma across the glomerular capillaries into Bowman's space and progresses through complex mechanisms of transtubular absorption and secretion.

The blood supply to the kidney is through the renal arteries. The main renal artery undergoes a series of branching within the kidney until the afferent arterioles are formed.

These give rise to the glomerular capillaries which in turn unite to form the efferent arteriole. The efferent arteriole then breaks up to form a peritubular capillary network. These join to form small veins which progressively unite to form the renal vein.

The glomerular filtration rate (GFR) for both the kidneys is the sum of the individual filtration rates of all the nephrons. GFR in a healthy adult is approximately 100-125 millilitres per minute. GFR can be accurately and conveniently measured by radionuclide methods.

Tubular function modifies the composition of the glomerular filtrate by processes of selective absorption and secretion, leading to the formation of urine. A great deal is now known about the resorptive and secretory functions of the various renal tubular segments which have important bearing on maintaining the electrolyte, acid base and fluid balance of the body. Established radionuclide methods are not yet available to study tubular function selectively; because a suitable radiopharmaceutical has not been developed for this purpose.

The collecting system, the pelvis, the ureters and the bladder are essentially concerned with the reservoir and transit functions for the urine formed in the kidney. Using suitable radionuclide techniques, it is possible to obtain qualitative and quantitative information regarding these functions.

**Basis of scintigraphic study.**

The radiopharmaceutical, when injected intravenously, is transported to the kidney through the renal artery and its branches. This phase of the transport of the radiopharmaceutical across the renal artery which may be termed the "arterial phase" lends itself very conveniently for imaging the renal arterial flow using a scintillation gamma camera. Significant obstruction to the blood flow through the renal artery or any of its major branches will be manifested as delayed appearance and diminished accumulation of the radioactivity in the whole or part of the kidney.

The functional unit of the kidney which is responsible for the discriminate handling of the injected radiopharmaceutical is the nephron. The radiopharmaceutical is passed into the tubular lumen through the glomerular filtration route. The factors which determine the route include:

(a) degree of protein binding

(b) molecular size and

(c) modecular charge.

On this basis, the kidney seeking radiopharmaceuticals are classified as glomerular agents (e.g. $^{99}Tc^{m}$ DTPA), tubular agents (e.g. $^{131}I$ Hippuran, $^{99}Tc^{m}$ MAG3, $^{99}Tc^{m}$ DMSA) and mixed type (e.g. $^{99}Tc^{m}$ GHA) (Table I).

TABLE I. COMMONLY-USED RADIOPHARMACEUTICALS FOR KIDNEY DISORDERS

| Radiopharmaceuticals | Biokinetics | Clinical application |
|---|---|---|
| $Tc^{99m}$-labelled compounds | | |
| 1. Diethylene triamine Pentaacetic acid (DTPA) | Negligible protein binding. Major renal route is glomerular filtration. Plasma clearance is slow. Renal clearance reflects GFR. Renal excretion is not fast. | Quantitation of GFR. Evaluation of urinary drainage, vesico-ureteric reflux, bladder function and urethral patency. |
| 2. Dimercapto succinic acid (DMSA) | Significant protein binding. Major renal route is tubular excretion, part by glomerular filtration,. Renal excretion is slow. | Overall assessment of kidney function. Imaging of kidney for focal renal abnormality such as scarring, infarction. etc. |
| 3. Glucoheptonate (GH) | Some protein binding. Excretion is through glomerular filtration and tubular excretion. Renal excretion is slow. | Same as for DMSA |
| 4. Mercapto acetyl triglycine (MAG3) | Significant protein binding. Major renal route is tubular. Behaves like orthoidodo-hippurate. Renal excretion fast. | Overall assessment of kidney functions. Evaluation of morphology of collecting system by imaging. May be used for assessment of renal tubular disorders. |
| $Tc^{99m}$ | Principal photon energy is 140 keV, good matching with gamma camera, physical half-life of six hours. Radiation dose to patients comparatively low, easily available, not expensive. so the most popular radiolabel. | |

TABLE I. (cont.)

| Radiopharmaceuticals | Biokinetics | Clinical application |
|---|---|---|
| Radioiodine-labelled compounds | | |
| 1. $^{131}$I orthoiodo hippurate | Significant protein binding. Major renal route is tubular excretion (80%) part by glomerular filtration (20%). Renal clearance reflects ERPF (effective renal plasma flow). Renal excretion is fast | Quantitation of renal plasma flow. Evaluation of upper urinary tract drainage. |
| 2. $^{123}$I orthoiodo hippurate | Significant protein binding. Major renal route is tubular excretion (80%) part by glomerular filtration (20%). Renal clearance reflects ERPF (effective renal plasma flow). Renal excretion is fast. | Quantitation of renal plasma flow. Evaluation of upper urinary tract drainage. Renal imaging for morphological evaluation. |
| $^{131}$I Principal photon energy is 360 keV, not a good match for gamma camera, poor quality images. Physical half-life is eight days, patient radiation dose is high. Easily available, not expensive. Mostly used for non-imaging probe studies. | | |
| $^{123}$I Principal photon energy is 160 keV, good match for gamma camera, good images. Physical half-life is 13 hours. Not easily available, very expensive. | | |

Once the radiopharmaceutical arrives in the tubular lumen, it flows along with the contents of tubular fluid and follows the flow of fluid within it, i.e. via the proximal convoluted and straight tubules, the descending and the ascending loops of Henle, the distal convoluted tubules to reach the collecting tubule. From there it flows on to papillary collecting ducts and to the minor and major calyces, where usually free mixing of radioactivity occurs with the urine contained in it. The sojourn of the radiopharmaceutical from the beginning to the end of the nephron can be referred to as the nephronal phase. This phase helps in obtaining the image of the kidney to study its gross morphology such as size, shape and position and presence of any intrarenal space occupying lesions. The image of the kidney obtained during this phase is the result of the collective function of all the nephrons. The image of the kidney defining the cortical part of the nephron can be termed "the cortical image". Occasionally, in the study of the kidney, it may be necessary to identify and separate these phases of the radiopharmaceutical transport in the kidney images. This can be useful in determining the transit time in different parts of the kidney, e.g. cortical transit time versus whole kidney transit time.

Renal transit time truly represents the time that it takes for the radiopharmaceutical, after its pulsed input into the renal artery, to travel through the tubules and collecting channels to reach the renal calyces. The factors which influence the transit time are:

(a) urine flow rate and

(b) the chemical nature of the radiopharmaceutical.

For a given flow rate, different renal radiopharmaceuticals can have different transit times. The amount of radiopharmaceutical present in a given kidney at the end of this transit time or during a fraction of this period is proportional to the function of the kidney. This fact is used in determining the relative function of the kidneys. The renal uptake of $^{99}Tc^{m}$ DTPA and $^{131}I$ OIH reflect the well defined renal functions like GFR and effective renal plasma flow (ERPF) respectively. The renal uptake of $^{99}Tc^{m}$ DMSA and $^{99}Tc^{m}$ GH reflect the function of the kidney, but do so without addressing any specific physiologic function.

As the urine, along with the radioactivity, collects in the renal pelvis, the pressure in the pelvis increases and initiates a peristaltic contraction beginning in the pelvis and spreading down along the ureter to force urine towards the bladder. A peristaltic wave occurs once every ten seconds to once every two or three minutes.

Once the radioactivity reaches the urinary bladder, it is usually so well and uniformly mixed with the urine in it, that bladder imaging is possible at this stage. The act of micturition forces the urine out through the urethra. The mucosal arrangement at the urethral orifices and the oblique course of the ureters through the wall of the bladder prevent the reflux of urine back into the ureters. The rate of disappearance of radioactivity in the bladder during the act of micturition provides valuable information regarding the detrusor function and patency of urethra, provided that there is no significant vesico-ureteral reflux. The radionuclide cystography and urine flowmetry have thus useful applications in clinical

urology. The dynamics of different renal radiopharmaceuticals, the renal functions which lend them for study, possible investigations and their indications are shown in **(Fig. 31.2)**.

### Common disorders of kidney and urinary tract

There are quite a few disorders of kidney and urinary tract which are commonly encountered in routine clinical practice. The frequency of occurrence of these disorders is more or less similar in many parts of the world with minor variations depending on environmental, hereditary and local factors.

The following is a list of these disorders wherein radionuclide investigations have proven value in diagnosis of the disease and management of the patient.

1. Obstructive uropathy/nephropathy
2. Urinary tract infection
3. Renal failure
4. Space occupying lesions
5. Renal/renovascular hypertension
6. Urinary tract injury
7. Congenital abnormalities
8. Renal transplant dysfunction (rejection, acute tubular necrosis, etc.)

It is quite possible, and indeed is the case in many patients, that two or more of these conditions co-exist and aggravate the harmful effects on the kidney.

### 1. Obstructive nephropathy/uropathy

This is perhaps the commonest disorder affecting the urinary tract and kidneys. The importance of this disorder lies in the fact that it is totally reversible when detected early and managed properly. It is in this context of early detection and proper management that the radionuclide tests have the greatest value. This is due to the very high sensitivity and specificity of the tests in identifying the obstruction. The obstruction can occur at any point in the urinary tract starting from the calyces of the kidney to the external urethral meatus. Such obstruction may be acute, subacute or chronic; unilateral or bilateral; and total or subtotal. The resultant rise in back-pressure may eventually lead to anatomical changes such as distension and dilatation of the collecting system proximal to the obstruction, and functional impairment of the nephrons leading to nephropathy and renal failure. It is

important to note that the very same investigations which are very useful in the early stages of the disease may prove least useful in the late stages of nephropathy and renal failure, as these tests basically study the function of the kidney. **Table II** gives the common causes leading to urinary tract obstruction.

**TABLE II. COMMON CAUSES OF URINARY TRACT OBSTRUCTION**

| Intrinsic causes | Extrinsic causes |
|---|---|
| Pelviureteric junction (PUJ) dysfunction<br>Vesico-ureteral dysfunction<br>Calculus disease<br>Neurogenic bladder<br>Bladder neck dysfunction<br>Infection<br>Urethral valves<br>Tumor<br>Trauma | Ureteral ligation during pelvic surgery<br>Tumour<br>Idiopathic fibrosis<br>Lymphocoele |

While there can be definite mechanical (organic) obstruction in many of the conditions listed in the table, it may be only functional in some such as vesico-ureteral reflux and neurogenic bladder. Dilatation of the renal calyces, pelvis, and ureter are common consequences of obstruction regardless of the cause and type of obstruction, i.e. mechanical or functional. In the case of the former, corrective measures are undertaken to remove the physical cause such as stone, stricture or tumour, while in the case of the later the attempt should be to correct the functional abnormality such as reflux or bladder dysfunction. Thus it is obvious that the proper management of the patient depends very much in distinguishing the type of obstruction and also in determining the extent of renal damage. Carefully selected radionuclide investigations can provide accurate information on both these aspects. Most other investigations such as plain X-ray, ultrasound and even computerised X-ray tomography give only anatomical information. Intravenous pyelography, rarely used in many centres after the advent of ultrasonography and radionuclide studies, also provides mainly anatomical information. But none of these non-invasive investigations can clearly distinguish the obstructed dilated urinary tract from the non-obstructed, but dilated tract. Radionuclide studies score over the others in this respect. The simplicity and safely inherent in radionuclide tests make them eminently suitable for repeat studies which form an important part in the management of patients with obstructive disorders prior to and following the corrective intervention.

Selection of radiopharmaceutical, while investigating obstruction, depends on the information required. The first question to answer is whether there is any actual obstruction or not, and the second question relates to the functional damage to the kidneys. The presence of obstruction is demonstrated by the continuously up-going second phase of the renogram curve and prolonged retention of radioactivity in the renal images. For this, it is better to use radiopharmaceuticals with relatively fast excretion such as $^{131}I$ OIH or $^{99}Tc^{m}$ DTPA. The function of the kidneys is better evaluated by the absolute uptake of $^{99}Tc^{m}$ DMSA. Deterioration of function as seen from serial studies is a definite indication for surgery to remove the obstruction.

Radionuclide studies should, therefore, be considered as a front-line investigation in the management of patients with urinary tract obstruction. Use of these studies as a stand-alone tests in certain clinical circumstances or as a complimentary test to others can be highly cost-effective in patient management.

## 2. Urinary tract infection

Urinary tract infection is a common problem in clinical practice. The group at risk for urinary tract infection (UTI) includes children, and patients having urinary obstruction, vesico-ureteral reflux, neurogenic bladder and diabetes mellitus. In one of the western countries, it is estimated that 1% of schoolgirls have asymptomatic bacteriuria and 5% of schoolgirls have proven UTI before they are ten years old. Around 10% of children with UTI will develop renal scarring at the time of first infection. Around 10-20% of children with scarring will subsequently develop hypertension. Between 50 and 60 adults per million develop renal failure every year and 15% of these are due to chronic pyelonephritis. Similar figures are not available for developing countries; if any, it will only show a higher incidence of renal damage due to UTI as a result of lack of awareness, late detection of disease and half-hearted or inadequate treatment of infection. If morbidity is to be prevented, it is necessary to keep a high index of suspicion, particularly in the high risk group, to diagnose the condition in time and to treat it adequately and vigorously.

Currently, out of the imaging modalities like intravenous pyelogram (IVP), ultrasonogram and radionuclide scan, it is the radionuclide scan using $^{99}Tc^{m}$ DMSA which is considered most sensitive in detecting renal scarring. There is a definite morbidity and mortality associated with the use of contrast media even with the newer, and more expensive non-ionic forms. The renal outlines may be difficult to see due to overlying bowel gas and scanty perinephric fat. Ultrasound in the child, even more than in the adult, is extremely operator-dependent. In principle, ultrasound does not involve ionising radiation, and should be used as the first investigation. But in view of the relatively high false negative rate of ultrasound, a negative examination should be followed by scintigraphy with DMSA. In any case the quantitative information on kidney function obtainable with DMSA is so unique that there is a strong case for performing this in every case of UTI, more so in the recurrent and chronic variety. Combined with other radionuclide methods such as renography, and radionuclide cystography it is possible to make a complete evaluation of the whole urinary tract to detect predisposing and correctable factors like obstruction, and vesicoureteral reflux, thus giving the

scintigraphic package a high index of cost effectiveness which is particularly relevant for developing countries.

## 3. Renal failure

There are many causes for renal failure and none may be apparent when the patient presents himself for the first time. The general aim of the radionuclide investigations in patients with renal failure is to assess the extent of the individual kidney damage and to look for clues to help in the management of the patient, both on a short term as well as long term basis. In every case of unexplained deterioration of renal function, whether acute or chronic, the possibility of urinary tract obstruction should receive careful consideration, because this, when detected and promptly treated, will save the kidney from further damage or even reverse the damage that had already occurred. The assessment of relative function of each kidney is also important as it provides management strategies for intervention.

As mentioned earlier, a combination of ultrasound and radionuclide studies has almost replaced the use of contrast intravenous pyelography (IVP). Using ultrasound, renal size and the degree of dilatation of the collecting system can be estimated by a competent and experienced investigator. If the ultrasound confirms that both kidneys are small and there is no dilatation of the collecting system, there is little to be gained by further imaging investigations; but if there is evidence of dilatation of the collecting system, then neither the ultrasound nor the IVP can distinguish between a non-obstructed dilated collecting system and an obstructed dilated one; neither can they assess the contribution of each kidney to the total function. In such a situation $^{99}Tc^{m}$ DTPA gamma camera renography (or $^{99}Tc^{m}$ MAG3 renography if available) or $^{131}I$ OIH sequential imaging should be performed; though with $^{131}I$ OIH the radiation dose to the kidney will be higher than that with $^{99}Tc^{m}$ compounds. Even when there is no dilatation, the scintigraphy should be performed, if the kidney size is different on both sides, to assess the relative function. It is important to continue the study for as long as twenty four hours, if sufficient information is not obtained earlier.

Imaging is of limited value in the differential diagnosis of the actual disease process. Small contracted kidneys suggest chronic renal damage which is not of obstructive origin and is likely to be irreversible. Large kidneys may suggest a variety of causes like polycystic, medullary sponge or amyloid kidneys, but most importantly obstruction.

$^{99}Tc^{m}$ DTPA is the most useful radiopharmaceutical for scintigraphic studies in patients with renal failure. Sequential images should be obtained at appropriate intervals for as long as necessary. Time activity curves (renogram) of the initial thirty minutes of the study may or may not be helpful in determining the presence of obstruction, particularly when the background radioactivity is quite high, in the initial phase. Increasing retention of radioactivity in the collecting system as seen in the delayed images is an indication of obstruction. If non-obstructed, the accumulated activity is usually faint, is in the cortical region and is only slightly higher than the background activity.

All patients with renal failure do not require scintigraphic investigations. They are indicated only in those patients in whom the ultrasonography has shown dilatation of the collecting system or it has failed to clearly visualise the collecting system. Scintigraphic study is indicated also in patients in whom asymmetrical kidney disease is suspected.

## 4. Space-occupying lesions (SOL) in kidney

Common causes of SOL in kidney include cysts (simple or hydatid), multicystic disease, polycystic disease, calculus, segmental hydronephrosis, segmental pyelonephritis, primary malignant tumours and haematoma. The name SOL suggests that the lesion displaces normal renal tissue. Renal radiopharmaceuticals, when administered, fail to get concentrated in the region occupied by the lesion. At the same time, it gets concentrated in the surrounding normal tissue thus the negative uptake in the SOL, commonly described as "cold area" in the scintigram, is the hallmark of the presence of SOL. While scintigram may be quite sensitive in the detection of SOL, it does not help in the differential diagnosis of the SOL.

Radiopharmaceuticals which do not change their distribution rapidly within the kidney and which mainly display cortical accumulation are preferred for imaging of renal SOL. $^{99}Tc^{m}$ DMSA and $^{99}Tc^{m}$ Glucoheptonate (GH) belong to this class of renal agents. Tracers like $^{99}Tc^{m}$ DTPA, $^{99}Tc^{m}$ MAG3 and iodinated OIH are far less satisfactory agents because of their short cortical residence time and rapid accumulation in the collecting system. The latter may mask the presence of SOL. A gamma camera fitted with a high-resolution collimator is the instrument of choice for scintigraphic imaging of SOL's. Magnified images using pin-hole collimator are useful particularly in infants and young children. Addition of a nuclear medicine computer will allow dynamic scintigraphy of renal perfusion phase, which may be useful in characterising some SOL's. Until recently, IVP using radiological contrast media was the front-line investigation of SOL. With the advent of ultrasound and X-ray CT, the use of IVP is receding. Scintigraphic imaging is to be regarded as complimentary to US or CT imaging or supplementary when additional information such as the effect of SOL on the renal function and urine flow is desired.

**Table III** gives the usual scintigraphic findings of various SOLs in the kidney in the three different phases of the scintigraphic study.

## 5. Renal/renovascular hypertension

Early in the course of hypertension, detection of kidney abnormality has important practical significance. Radionuclide studies have been shown to have very high sensitivity, specificity and accuracy in detecting the presence of renal disease, especially when unilateral. When the radionuclide tests indicate renal disease in a patient with hypertension of recent onset, it is quite likely that the hypertension is renal. The nature of the disease can be determined by further investigations. On the other hand, if the kidneys are found to be normal after the radionuclide tests, renal causes can be excluded for the hypertension. Thus radionuclide tests have a well recognised role as a screening test for hypertension, particularly in children, young adults or in older people and when kidney disease is suspected.

TABLE III. USUAL SCINTIGRAPHIC FINDINGS IN SOL IN THE KIDNEY

| S.No. | Pathological entity | Renal scintigraphic findings | | |
|---|---|---|---|---|
| | | Perfusion phase | Early cortical and collecting system phase | Delayed cortical and collecting system |
| I | II | III | IV | V |
| 1. | CYSTS (simple, hydatid) | Hypoperfusion, avascular appearance. | Focal photon deficient area. "Cold" lesion usually solitary and cortical location. | Same as the early phase. |
| 2. | Multicystic disease | Same as above, involving multiple areas. | Same as above, but multiple. Usually unilateral. | Same as early phase. |
| 3. | Polycystic kidney (adult) | Same as above. Usually Bilateral. | Large kidneys. Same as above. Usually bilateral and multiple. | Same as early phase. |
| 4. | Calculus disease (with kidney function preserved) | Normal cortical perfusion. | Normal cortical uptake. Photon deficient area in the major collecting system corresponding to large stone. | Normal cortical uptake "Fixed" photon deficient area in the collecting system with evidence of statis or obstruction. |
| 5. | Hydronephrosis | Generally shows diminished renal perfusion, the degree of decrease quite variable. Perfusion images show large central void due to distended collecting system (transient) | Cortical activity depends on overall renal function. Gradual appearance of radioactivity in the previously photon deficient central void. | Increasing activity in the collecting system. |

TABLE III. (Cont.)

| S.No. | Pathological entity | Renal scintigraphic findings | | |
|---|---|---|---|---|
| | | Perfusion phase | Early cortical and collecting system phase | Delayed cortical and collecting system |
| I | II | III | IV | V |
| 6. | Primary renal neoplasms (renal cell carcinoma) | Hyperperfusion. Hyper-vascular in appearance. | Focal decreased cortical uptake. Usually solitary | Same as early phase. Multiple lesions reduce the chance of primary carcinoma. |
| 7. | Renal infarct | Focally decreased perfusion. | Cortical uptake defect. | Same as early phase, but better delineated. |
| 8. | Renal trauma (hematoma, tear) | Focally decreased perfusion. | Uptake defect depending on the location of the lesion - cortical or central. | Same as early phase. |
| 9. | Pyelonephritis (unifocal or multifocal) | Diminished perfusion. | Focal cortical uptake defect - single or multiple. | Same as early phase. |
| 10. | Renal abscess | Diminished focal perfusion. | Focal cortical uptake defect. | Same as early phase. |
| 11. | Renal pseudo-tumour (hypertrophic columns of Bertin). | Normal perfusion. | Normal cortical uptake. | Normal cortical uptake. |
| 12. | Renal transplant (segmental ischaemia may be seen in a normally functioning or rejecting transplant). | Diminished focal perfusion | Focal cortical uptake defect. | Same as early phase. |

Renovascular hypertension (R.H.) occurs in about 5% of the population with hypertension. Correct diagnosis of this condition is important because it is curable if detected in time. The use of the term renovascular hypertension implies that the narrowing of the renal arteries is causally related to the elevation of the arterial blood pressure and re-establishment of adequate blood supply results in the cure of hypertension. Atherosclerosis, fibrodysplasias and aortoarteritis involving renal arteries account for about 99% of cases of renovascular hypertension. One of the mechanisms which sustain hypertension in this disease is mediated through renin-angiotensin system, particularly in the early stages. The renin-angiotensin dependence of hypertension can be elucidated by the administration of an angiotensin-converting enzyme inhibitor called Captopril.

This forms the basis of using a Captopril renogram for the diagnosis of renovascular hypertension.

Various radionuclide techniques like probe renography, dynamic sequential imaging and clearance studies (GFR, RPF) have been used for the diagnosis of R.H. These investigations can be carried out in a nuclear medicine department which has a gamma camera, computer and appropriate software. The usual parameters of kidney function useful in patients of R.H. relate to renal blood flow (renal perfusion index), renal uptake function reflecting GFR or RPF as the case may be, and urine flow rate reflected by retention of radioactivity or abnormal transit time. However, the abnormalities in these parameters are not only seen in patients of R.H., but they are also seen in patients with other kidney diseases such as urinary obstruction, pyelonephritis and renal hypoplasia. Also, easy recognition of these abnormalities requires that the renovascular disease be confined to only one kidney and that the contra-lateral kidney be normal for reference and comparison. These shortcomings of the conventional radionuclide renal studies can be overcome by doing interventional studies, notably a Captopril renogram. Based on the mechanism of Captopril intervention, it is claimed that a Captopril renogram not only adds some degree of certainty to the diagnosis of R.H., but it also provides prognostic information regarding the beneficial outcome of therapeutic measures like balloon angioplasty and revascularisation surgery.

The sensitivity of rapid sequence IVP is also in the region of 70-80%. More sensitive and specific diagnostic tests like renal vein renin estimation and split renal function after ureteral catheterization are invasive and therefore cannot be considered for screening purposes. Digital substraction angiography has not been widely available as yet. Considering the simplicity, safety and accuracy, a Captopril renogram can be considered as a screening test for R.H. before sending the patient for selective renal arteriography.

## 6. Urinary system injury

Accidents and incidents causing morbidity and mortality to human life are on the increase. Road accidents, civil disorders, industrial accidents, building collapse, assault and natural calamities like earthquake and flood add to the overall incidence of accidents. Although head injury forms the major cause of death in such cases, abdominal trauma and injury to the urinary tract contribute significantly to the morbidity and mortality among the

victims of accidents. With the remarkable improvement in the practice of nephrology, early detection and proper management of such injuries can save many lives.

The successful management of patients with renal injury requires:

(a) recognition of the site of injury;

(b) assessment of individual renal function; and

(c) identification of any pre-existing renal disease.

Currently IVP and US scanning are considered front-line investigations in these patients. IVP is known to underestimate as well as overestimate the extent of injury. It cannot assess renal perfusion. In seriously-ill patients, it may be difficult to prepare the case for an IVP (bowel preparation) when the test needs to be carried out in an emergency. Ultrasonography, though very useful in detecting lacerations and haematomas, provides only limited information on renal perfusion and function. Functional evaluation of the individual kidney has a pivotal role in the management of patients with major renal injury but in stable clinical status.

Injury to renal vessels is one of the major factors which dramatically alter the therapeutic approach in patients with kidney injury. A normal $^{99}Tc^{m}$ DTPA dynamic study showing good and symmetrical renal perfusion rules out any major vascular injury. In patients with significant vessel injury, no perfusion or concentration of radioactivity is observed in the affected kidney. Transient vascular spasm leading to non-perfusion can be detected by appropriately timed serial studies. Assessment of relative function of the kidneys serves to form guidelines for further management. Clinically stable patients having moderate to good renal function may be treated conservatively; and unstable patients with moderate to poor function usually need surgical intervention. In short, there are good reasons to recommend radionuclide investigation to be part of frontline investigations in patients with known or suspected injury to the urinary system.

## 7. Congenital abnormalities

The various congenital abnormalities include:

(a) Congenital cystic disease (polycystic disease, medullary sponge, simple cysts)

(b) Horseshoe kidney

(c) Crossed renal ectopia

(d) Pelvic kidney

Usually, these abnormalities are detected as incidental findings while investigating the kidneys for other reasons. Congenital defects associated with malpositioning such as

horseshoe, ectopic and pelvic kidney render them prone to obstruction, infection and urinary stone formation. When ectopia is suspected and only one kidney is visualized, it is important and rewarding to specifically look for the other one by doing imaging at different projections (such as anterior view) and sites (pelvis). Radionuclide studies can play a significant role in the functional evaluation of the ectopic kidney; at times it can play a very useful role in locating the abnormally placed kidney that has eluded the search by ultrasound and radiological contrast studies.

## 8. Renal transplant dysfunction

Transplanted kidney is constantly under threat and has to struggle for survival. The very measures that protect it from the immune mechanisms of the host are potentially toxic and weaken the defences against infection. Accidents associated with transplant surgery such as ureteric ligation add further risk to its survival. Early detection and treatment of conditions which affect the transplant are crucial. Radionuclide techniques have been shown to be eminently suitable for renal transplant surveillance and evaluation. The common complications of renal transplant are:

(a) Ischemia
- Vascular obstruction
- Acute tubular necrosis

(b) Immunological
- Hyperacute, acute and chronic rejection

(c) Toxic
- Cyclosporin toxicity

(d) Urinary complications
- Leak, lymphocoele, obstruction

(e) Infection

All efforts should be made to evaluate critically any diagnostic procedure in terms of potential hazard to the transplant and the cost-effectiveness of the investigation. Because of the immune suppression, transplant patients are at a higher risk of infection. Catheterization, endoscopy, contrast angiography and allograft biopsy carry significant risk in these patients. IVP may not be very helpful in patients with diminished allograft function. Ultrasound examination is highly suitable in these patients to study structural abnormalities related to transplant dysfunction, it may be difficult to do US in the immediate post-operative period because of the bandages, wound, clips, sutures etc. It cannot also depict real time functional abnormalities which accompany the altered structure. Please note that in acute rejection and acute tubular necrosis, functional alterations are more prominent than structural alterations, if any. It is in the context of detecting real time functional abnormalities with virtually no

risk to the patient that radionuclide evaluation of renal transplant has gained wide acceptance in clinical practice.

Many centres in developing countries still use probe renography system and $^{131}$I-OIH for performing renography. Probe renogram curves and blood clearance index of $^{131}$I-OIH have been used for assessment of renal transplant function. A single study may not yield the required diagnostic information, but information regarding transplant dysfunction can be best obtained from serial studies in the same patient. It may also be not possible to derive at a differential diagnosis, hence differential management, of the various conditions which can affect the transplanted kidney. The main value of probe renogram study is in documenting the change of function serially during the life of a graft.

The gamma camera and a suitable data processing system (computer) is the instrument of choice. $^{99}Tc^{m}$ DTPA is currently the radiopharmaceutical of choice, since it can provide good quality images of all phases of renal transplant function such as perfusion, renal uptake and renal excretion. It also serves to study the function of the lower urinary tract and urinary bladder.

The renal transplant evaluation, using the gamma camera computer system, consists essentially of a dynamic first pass study followed by dynamic sequential scintigraphy. Static imaging of the entire region using a high resolution collimator at appropriate intervals helps in identifying morphological abnormalities (SOL's) that are suspected during the dynamic phase of the study. At times, it may be necessary to obtain delayed images even at 24 hours.

The first-pass scintigraphy helps in detecting significant obstruction to the blood flow to the transplant. Poor perfusion indicates renal artery or renal vein thrombosis. Total absence of perfusion can be due to renal infarction or hyperacute rejection which necessitates removal of the transplant. Quantitative parameters such as transplant perfusion index, not only serve to detect perfusion abnormalities, that are not well appreciated visually, as is the case sometimes with acute rejection, but also serve to document quantitatively changes in renal perfusion in follow-up studies. Sequential dynamic scintigraphy provides information on the uptake and excretory function of the transplant. It is possible to differentiate acute rejection and acute tubular necrosis at this stage. Normal perfusion, near normal uptake and delayed excretion are typical of early phases of acute tubular necrosis, whereas diminished perfusion, low uptake and delayed excretion characterise acute rejection. Bladder activity is better seen in cases of acute rejection than in cases of acute tubular necrosis. Transplant perfusion index is almost always abnormal in acute rejection and normal in early cases of acute tubular necrosis. Urinary outflow tract obstruction is easily diagnosed by continuous accumulation of activity in the transplant and poor activity in the urinary bladder. Delayed static images are very helpful in detecting and identifying space occupying lesions such as urinoma, lymphocoele, urinary extravasation and abscess. Transplant dysfunction, in the absence of such usual complications as acute rejection and acute tubular necrosis may be due to drug toxicity (Cyclosporin toxicity). Needless to say that the information obtained from radionuclide investigations has to be evaluated in the light of the overall clinical picture of the patient.

Radiopharmaceuticals such as $^{99}Tc^{m}$ sulphur colloid and $^{123}I$ fibrinogen have been used to differentiate acute rejection from acute tubular necrosis. A kidney being rejected accumulates these radiopharmaceuticals whereas the kidney with acute tubular necrosis does not.

## 9. Reflux nephropathy

Vesicoureteral reflux (VUR), i.e. retrograde flow of urine from the bladder into the ureters and upper urinary tract, is not an uncommon disorder. This phenomenon may be congenital or acquired. When VUR is congenital and not associated with other defects such as bladder neck obstruction and urethral valves, it may regress and spontaneously disappear with time. When the VUR reflux is associated with the above-mentioned defects of the lower urinary tract, it may progress relentlessly and result in functional and structural changes in the kidney and upper urinary tract. Structural abnormalities may include dilatation of calyces and ureters and scarring of the kidney following episodes of infection. These patients are at higher risks for urinary infection and repeated episodes of infection and consequent scarring may lead to renal failure termed reflux nephropathy. Acquired VUR can be seen in patients who have undergone ureter implantation surgery.

Adequate evaluation of patients with VUR remains a challenge. The diagnosis of VUR has been traditionally dependent on X-ray micturating cystourethrograms (MCU). Over the past two decades, several investigators have shown that radionuclide MCU using a gamma camera computer system and $^{99}Tc^{m}$ DTPA is more reliable and sensitive in detecting VUR than X-ray MCU.

Spot film X-ray MCU requires catheterization. It provides excellent anatomical details of the urinary system, but it gives more radiation to the gonads and involves added risk of infection in these patients in whom infection is to be avoided. It is also less sensitive in detecting VUR, especially when the reflux is intermittent. Radionuclide MCU overcomes many of these shortcomings of X-ray MCU and is ideal for repeat studies as it is non-invasive and involves less radiation to the gonads. For these reasons, it is particularly suitable in paediatric patients - the group which has the maximum incidence of VUR.

Radionuclide MCU can be performed in two ways, one as a follow-up of procedure of a $^{99}Tc^{m}$ DTPA renographic study. Following the renographic study, sufficient time is given for the radioactivity to accumulate in the bladder before performing the radionuclide MCU. The other method is to introduce radioactivity directly into the bladder either through a catheter or through a suprapubic puncture of the bladder. The first method is called indirect radionuclide MCU and the second method is called direct radionuclide MCU. In the author's experience, direct radionuclide MCU through the suprapubic puncture of the bladder using a disposable hypodermic needle has been simpler and risk-free. A direct radionuclide cystogram provides, in addition to the demonstration of VUR, quantitative indices like initial bladder volume, residual bladder volume, refluxing volume, maximum and minimum urine flow rate during the act of micturition. These are important parameters while evaluating a patient with VUR before or after the treatment.

VUR can be graded I-V, depending on the extent of retrograde urine flow and the structural alterations of the upper urinary tract induced by the reflux.

## COMMON RADIONUCLIDE INVESTIGATIONS

1. Static renal imaging
2. Dynamic renal imaging
3. Quantitative estimation of GFR/RPE
4. Probe renogram (non-imaging)
5. Interventional studies
6. Cystourethrogram and urine flowmetry.
7. First pass renal angiography

### 1. Static renal imaging

Indications

(a) Assessment of mass lesions (cysts, tumours, pseudotumours)

(b) Congenital abnormalities (fusion, ectopia)

(c) Assessment of function (divided, regional)

(d) Detection of renal scarring (following infection)

$^{99}Tc^{m}$ DMSA is the radiopharmaceutical of choice for static renal imaging, since it is fixed to the kidney parenchyma for a long period, $^{99}Tc^{m}$ GH (glucoheptonate) is also used, but is not as good as DMSA.

Procedure for $^{99}Tc^{m}$ DMSA/GH static gamma camera imaging

(a) Prepare a dose of $^{99}Tc^{m}$ DMSA or $^{99}Tc^{m}$GHA. The adult dose is about 185-259 MBq (5-7 mCi). For children 74-185 MBq (2-5 mCi) of radioactivity should be used.

(b) Set up the gamma camera for $^{99}Tc^{m}$ with a low energy, high resolution, parallel hole collimator.

(c) The radioactivity is administered intravenously and renal imaging is done at 15 minutes, 30 minutes, 1 hour, 2 hours and at 4 hours. If necessary, a scan should also be done at 24 hours in patients with poorly functioning kidneys.

(d) Isotime renal imaging is done both in the anterior as well as in the posterior projection. Oblique views can be taken wherever necessary. (Isotime = Note the time taken to collect sufficient counts to get a good image in the anterior projection, and use the same time for all other projections.)

(e) Certain useful guidelines should be followed at the time of interpreting a static renal scan.

(i) Observe the site, size and shape of the kidneys. Look for any asymmetry in size, abnormality in shape, irregular outline, etc.

(ii) Observe qualitatively the degree of radionuclide concentration in each kidney.

(iii) Observe the distribution of radioactivity in the renal parenchyma. Look for evidence of scarring, SOL, dilated pelvicalceal system and upper urinary tracts. Multiple, focal cortical uptake defects are suggestive of scarring.

(f) For the calculation of relative renal function, ideally the delayed images obtained at four hours are taken into consideration, and the calculations are done using a region of interest (RIO) selector and appropriate software.

(g) (i) First the posterior view is analyzed. ROIs are selected over the right kidney (RIO 1), left kidney (RIO 2), background below the right kidney (RIO 3) and background below the left kidney (RIO 4).

(ii) The areas of RIO 1 and RIO 3 are first normalized followed by normalization of areas of RIO 2 and RIO 4. Using the normalized counts, the renal concentration of radioactivity is calculated for each kidney as follows:

**Net cts.in rt kid. in post.view = cts.in rt kid. - Normalized bkg. cts.**
**Net cts.in lt kid. in post.view = cts.in lt kid. - Normalized bkg. cts.**

(h) Similarly, the anterior views are also analyzed and net counts in both kidneys are calculated.

(i) The following data are now at our disposal:

Net counts in right kidney in the posterior view (RP)
Net counts in right kidney in the anterior view (RA)
Net counts in left kidney in the anterior view (LA)
Net counts in left kidney in the posterior view (LP)

(j) Percentage function of each kidney can be calculated by using the following formula:

$$\textit{\% Function right kidney} = \frac{\sqrt{(RP \times RA)}}{\sqrt{(RP \times RA)} + \sqrt{(LP \times LA)}} \times 100$$

$$\textit{\% Function left kidney} = \frac{\sqrt{(LP \times LA)}}{\sqrt{(LP \times LA)} + \sqrt{(RP \times RA)}} \times 100$$

## 2. Dynamic renal imaging

Indications

(a) Assessment of renal function (divided, regional)

(b) Assessment of dilated upper urinary tract (obstruction versus non-obstruction)

(c) Obstructive uropathy

(d) Vesicoureteral reflux

(e) Assessment of renal transplant function/complications

(f) Assessment of renal blood flow

Dynamic scintigraphy is done mostly using $^{99}Tc^{m}$ DTPA and gamma camera computer system. $^{99}Tc^{m}$ MAG 3 has been recently introduced, as replacement for iodinated Hippuran. MAG 3 (Mercapto acetyl triglycine) is a tubular agent.

Procedure for $^{99}Tc^{m}$ DTPA/MAG 3 gamma camera renography.

(a) Prepare a dose of $^{99}Tc^{m}$ DTPA or $^{99}Tc^{m}$ MAG3. The adult dose is normally about 185-259 MBq (5-7 mCi). For children, 74-185 MBq (2-5 mCi) of radioactivity should be taken.

(b) Set up the gamma camera for $^{99}Tc^{m}$ with the low-energy high-resolution parallel hole collimator or a low-energy all-purpose (LEAP) collimator.

(c) Position the patient for renal dynamic study. Normally, the study is performed

with the patient lying supine on the examination table with the detector placed below the patient. Ideally the renal area should be in the centre of the field of view of the detector.

(d) Set the computer ready to acquire data in frame mode.

(e) Administer the radioactivity intravenously into the patient as a bolus and simultaneously activate the computer. Acquire data in frame mode, in a total of 127 frames.

(f) Depending upon the information required, the acquisition of data can be made either uniformly (time per frame - 16 seconds for all 127 frames) or by applying the variable time acquisition facility (time per frame - 1 second for first 40 frames, followed by time per frame - 16 seconds for the rest of the frames).

(g) At the end of acquisition, examine the serial images frame by frame. Select regions of interest (RIO) over right kidney (RIO 1), left kidney (RIO 2), abdominal aorta (RIO 3) and background (RIO 4). Whenever necessary additional RIO's may also be selected over the ureters and the urinary bladder. Area normalized and background subtracted time activity histograms are obtained over the selected RIO's.

(h) Routinely, an X-ray printout of the serial images, selected RIO's, and time activity histograms along with the annotations are obtained for reporting and record.

**NOTE: The study can be suitably modified to evaluate the single transplanted kidney.**

### 3. Quantitative estimation of renal function (GFR/RPF)

Indications

Individual kidney function in unilateral or asymmetric bilateral renal disease:

(a) as a baseline parameter for future reference

(b) to decide about nephrectomy or salvation surgery

(c) for prognosis regarding beneficial effects of nephrectomy, in renal artery stenosis and hypertension

## 3A. GFR determination

Procedure for determination of GFR

(a) Prepare weighed dose of 74 MBq of a stock solution of $^{99}Tc^{m}$ DTPA and weighed standard of 74 MBq. Calculate the dose/standard ratio (correction factor - CF) from their net weights.

(b) Dilute the standard to exactly one litre (note the dilution factor - DF).

(c) Inject the dose intravenously. Note the time.

(d) Take 6 ml heparinized blood samples at 1.5, 2, 2.5, 3. 3.5 and 4 hours post-injection, again noting the actual collection time.

(e) Centrifuge the blood samples.

(f) Dispense 1 ml samples of plasma and diluted standard solution into labelled sample tubes.

(g) Measure the activity of each sample, using a scintillation well counter calibrated and set up for $^{99}Tc^{m}$.

(h) Using a semilog (log-linear) paper, plot the plasma activity as a function of time. Find the best straight line fit to these data and extrapolate the line to zero time. Note the extrapolated activity at zero time. Calculate the half time of clearance (T½).

(i) Calculate GFR by using the principle of single exponential analysis.

(j) First calculate the volume of dilution (V) as follows:

$$V = \frac{\text{Injected dose}}{\text{Plasma activity at 'O' time}}$$

$$= \frac{\text{Activity diluted standard x DF x CF}}{\text{Plasma activity at 'O' time}}$$

(k) Now calculate GFR as follows:

$$\text{GFR} = \text{Volume of dilution x clearance constant (Ml/min)}$$

$$= V \times \lambda \quad \text{(ml/min)}$$

$$= \frac{V \times 0.693}{T½} \text{ (ml/min)}$$

**Note: Decay corrections for $^{99}Tc^{m}$ may be applied wherever necessary.**

## 3B. Determination of renal plasma flow (RPF)

Procedure for calculation of RPF

(a) Prepare a weighed dose of 1.85 MBq of a stock solution of 131I Hippuran and weighed standard of 1.85 MBq. Calculate the dose/standard ratio (correction factor - CF).

(b) Dilute the standard to exactly one litre.

(c) Inject the dose intravenously.

(d) Take 4 ml heparinized blood samples at 10 minutes interval up to 60 minutes using a site other than that used for the injection of radioactivity and note the collection time of each sample.

(e) Centrifuge the blood samples.

(f) Dispense 2 ml samples of plasma and diluted standard solution in labelled sample tubes.

(g) Measure the activity of each sample using a scintillation well counter set up for $^{131}I$.

(h) Using a semilog (log-linear) graph paper plot the plasma activity as a function of time. Calculate RPF by using the principle of biexponential analysis and the following formula:

$$\text{RPF} = \frac{\lambda 1\ \lambda 2 \times \text{dose injected}}{A\lambda 2 + B\lambda 1} \text{ ml/min)}$$

$$= \frac{\lambda 1\ \lambda 2}{A\lambda 2 + B\lambda 1} \text{ X Counts in diluted standard X Dilution factor X Correction factor CF (ml/min)}$$

Using curve splitting, separate the slow component from the fast component.

$\lambda 1$ - slope of slow component
$\lambda 2$ - slope of fast component
A - Zero time intercept of $\lambda 1$ at the activity axis
B - Zero time intercept of $\lambda 2$ at the activity axis

## 4. Probe renogram.

Indications

(a) Qualitative assessment of individual kidney function.

(b) Detection of obstructive uropathy, particularly acute obstruction.

(c) Assessment of dilated upper urinary tract (obstruction versus non-obstruction).

(d) Assessment of renal transplant function.

The radiopharmaceutical used is $^{131}I$ OIH and the instrument is a multiprobe (minimum two probes) scintillation detector and strip chart recorder for recording the time activity curves (complete renography system).

Procedure

Radio-Hippuran renogram

A radio-Hippuran probe renogram is the most common technique for recording the renogram, where a simple dual probe system is used. Two matched sodium iodide scintillation detectors through the standard system of electronics are connected to ratemeters, which in turn are connected to chart recorders. The chart recorders produce graphs of activity in the kidneys with respect to time following intravenous bolus injection of $^{131}I$ Hippuran. Additional information may be obtained from other detectors placed over the urinary bladder and the left infra-clavicular region.

Since the renogram records $^{131}I$ accumulation in the renal area, it is obvious that the position of the detectors has an important effect on the shape of the tracings obtained. Precise placement of the probes is a critical step in this study and wrong probe placement may lead to false positive results. In normal practice, before each study, the surface marking

of the patient's kidneys are drawn and the probes are placed in apposition to them. Some centres use a small pilot dose of $^{131}I$ Hippuran to locate the kidneys before injecting the major portion of activity for the renogram.

The patients generally do not require any preparation. It is a good practice to ensure that patients drink enough water and empty their bladder before starting the renogram. These two precautions will minimize false positive renograms mimicking outflow obstruction by dehydration and back pressure from a full bladder. It is better to avoid doing renograms soon after intravenous urography or angiography.

The test is usually performed with the patient sitting. Most patients do not have any difficulty in maintaining the posture for the duration of the test which is about twenty minutes. But this does not apply to sick patients and infants in whom the test is performed in prone position. A mild sedation may be necessary in young children and un-cooperative adults.

After the patient is positioned 2.2-3.7 MBq (60-100 microcurie) of $^{131}I$ Hippuran is injected intravenously into the antecubital vein as a tight bolus. Simultaneously the chart recorder is activated. Normally the study is conducted for a period of 20 minutes. The volume of the injected activity should be as small as possible in order to obtain a good bolus function and the injection must be accurate, since any extravasation will produce a flat curve due to slow and continued absorption of the tracer from the subcutaneous tissue.

The renogram curve.

The normal renogram performed in this way shows three classical phases **(Fig. 31.3)**. The first phase consists of a rapid rise in count rate during the first minute after injection. It corresponds mainly to the radioactivity in both the extra renal and renal vascular beds within the first few seconds following intravenous injection of $^{131}I$ Hippuran. After few seconds this gives way to a more gradual slope, the second phase, which corresponds chiefly to the renal handling of the Hippuran as it is extracted by the tubular cells and passed to the lumen of the tubules. In a normal well-hydrated subject, the second phase rises towards a maximum, the peak, which occurs 2.5 to 4.5 minutes after the injection. The shape and the duration of this part of the curve are dependent on several factors: renal blood flow, tubular extraction efficiency, intraluminal transit and forward drainage. The rising curve is due to the fact that more and more Hippuran is arriving at the kidney through recirculation while none has left the renal pelvis. The period of declining amplitude after the peak is the third phase of the renogram. In this phase, more radioactivity leaves the renal pelvis than what is arriving in it. The beginning of the third phase of the renogram corresponds to the time at which activity first appears in the bladder. The third phase of the renogram curve reflects predominantly the drainage function of the kidney. In normal subjects the slope of the third phase usually begins to plateau near the base line about 20 minutes after intravenous injection.

Each phase of the renogram is determined by a number of simultaneously occurring intra- and extra- renal activities. The overlapping of these multiple physiologic processes determine the shape of the renogram curve but precludes the separation of the individual contributing factors. Because of the difficulty in separating these factors, and the changes in their relative contribution to the three phases of the renogram, it is not possible to quantitate the physiological parameters of renal function from the analysis of the curve. In spite of all these limitations, the renogram still provides a truly functional assessment of the kidney and upper urinary tract. It provides useful information in various renal disorders, such as obstructive uropathy (**Fig. 31.4**), nephropathies of various etiologies (**Fig. 31.5**) and renovascular hypertension (**Fig. 31.6**).

Renogram curve interpretation

Certain useful guidelines should be followed at the time of interpreting a renogram curve. They are as follows:

(a) First, observe the deviation from the normal pattern of the renogram curve.

(b) Translate these deviations to possible alterations in the physiology of the kidney in terms of blood flow, kidney uptake function, urine flow rate and drainage function.

(c) Such derived information as to the changes in kidney physiology is useful in providing differential diagnosis.

(d) The most probable diagnosis is selected out of the differential diagnosis on the basis of the clinical setting of the patients's disorder.

(f) It may be pointed out that a renogram curve should not be used primarily to pinpoint a diagnosis, but should be used mainly to identify the altered kidney physiology as a result of the disease in the patient.

## 5. Interventional techniques

(a) Diuresis renography

Increased urine flow caused by diuresis overcomes simple stasis and helps in clearing the radioactivity from the upper urinary tract. On the other hand, if the stasis is due to true mechanical obstruction, increased urine flow cannot overcome the hold-up and the radioactivity tends to accumulate in the urinary tract proximal to the obstruction. This is the principle underlying the diuretic intervention. The urinary tract may or may not be dilated depending on whether the impediment to urine flow is chronic or acute. It has been shown that diuresis renography can distinguish between dilated obstructed upper urinary tracts from dilated non-obstructed ones - an issue that cannot be resolved by other investigations like ultrasound, IVP and X-ray CT. It is important to realise that the predictive value regarding

the presence of obstruction is closely related to the function of the kidney. Good function increases the predictive value and poor function decreases it.

There is no consensus regarding the time of diuretic intervention as to whether it should be before the start, at the beginning or in the middle or at the end of the renograpy procedure. The most commonly used diuretic is Frusemide administered intravenously in the dose range of 0.3-0.5 mg/kg body weight. It is important to standardize the technique, validate it, and establish values for different groups of patients, so that the interpretation of the test has a meaningful basis.

Following diuresis, a significant decline in the third phase of the renogram curve rules out any organic obstruction and the need for any urgent therapeutic measures. Absence of a significant fall in the third phase indicates obstruction and the need to watch that kidney closely and to undertake measures to remove the obstruction and save the kidney from further damage. Attempts to quantitate the decrease or the change in radioactivity following diuresis have given rise to various indices such as diuretic index, and diuretic excretion index, etc., which help in interpreting the results and in monitoring the changes with time and with treatment more objectively.

In situations of compromised renal function, ( such as sub-total/partial obstruction, equivocal or low-grade pelviureteric functional stenosis, grossly dilated pelvicalyceal system, immediate post-operative period, and severe vesicoureteric reflux), the test may give results which may be difficult to interpret unequivocally.

(b) Captopril renography.

In renovascular hypertension, the elevated systemic arterial blood pressure is sustained in the early stages mainly through the renin-angiotensin mechanism. Angiotensin I is converted to angiotensin II, which is a powerful vaso-constrictor, by the angiotensin-converting enzyme (ACE) present in lungs.

Captopril is used as an antihypertensive drug. It acts by inhibiting the ACE and thereby blocking the production of angiotensin II. In the kidney with a stenotic renal artery, filtration at the glomeruli is maintained by vaso-constriction of the efferent arterioles sustained by angiotensin II. Captopril relieves this vaso-constriction, resulting in a fall of glomerular filtration. This is the pathophysiological mechanism underlying Captopril intervention and the principle of Captopril renography.

Demonstration of a decrease in the renal uptake of $^{99}Tc^{m}$ DTPA by the kidney with a stenotic artery following Captopril administration indicates that the renal artery stenosis is functionally significant in triggering the renin-angiotensin mechanism responsible for hypertension. When iodinated OIH or $^{99}Tc^{m}$ MAG3 is used, there is progressive accumulation of radioactivity in the kidney with the stenotic artery due to prolongation of transit time. This is also considered to be the result of shutting off glomerular filtration by Captopril administration.

Captopril is administered orally, in the dose of 25-50 mg for the adult patient, one hour before the renographic procedure. Haemodynamic parameters like pulse and blood pressure of the patient are regularly monitored until they become stable. Hypotension and transient renal failure (pre-renal) are occasional complications. Adequate volume replacement by intravenous fluids takes care of these complications.

It is believed that a Captopril renogram is more sensitive in the diagnosis of renovascular hypertension than the conventional one. It is also considered to indicate the outcome of revascularization procedures to establish adequate blood supply to the kidney. A positive Captopril test suggests successful results after revascularization. As the test is new, these observations are based on few studies, and there is a need to substantiate these by larger experience with Captopril renography.

## 6. Cystourethrogram and urine flowmetry

Evaluation of bladder function and urethral patency had not received much attention from nuclear medicine specialists so far. This had largely been due to lack of demand from the urologists who were not made aware of the potentials of nuclear medicine techniques in this field. This situation is slowly changing. Nuclear medicine techniques for the evaluation of urinary bladder functions are becoming popular especially with the paediatric urologists, mainly because of the sensitivity, accuracy and unmatched safety and simplicity.

A cystourethrogram essentially demonstrates the distribution and kinetics of radioactivity in the bladder during different phases of its function, i.e. filling and micturating phases. This helps in detecting vesico-ureteral reflux (VUR) and in measuring urine flow rates at given bladder volumes. This has been found to be very useful in the management of patients with VUR, neurogenic bladder, bladder neck obstruction, posterior urethral valves and urethral stenosis.

The radioactivity in the bladder can be from the renographic study using $^{99}Tc^{m}$ DTPA, if the cystourethogram is planned soon after (indirect radionuclide cystourethogram - IRCG). Radioactivity can be also directly introduced into the bladder either through a urethral catheter or through a suprapubic puncture of the urinary bladder by a needle (direct radionuclide cystourethrography - DRCG). Both have certain advantages and disadvantages; DRCG is described in some detail here as it is the procedure favoured by the author.

DRCG by suprapubic puncture is more physiological than a conventional X-ray micturating cystourethrogram (MCU) and catheter-aided DRCG. It avoids complete emptying and refilling of the urinary bladder.

Technique

In performing direct radionuclide cystogram (DRCG) and urine-flowmetry (UFMT), the patient is permitted normal activity prior to the examination. Primary requirement is a

reasonably full urinary bladder. The patient is encouraged to drink a lot of water and if he/she is able to hold urine, the patient is instructed not to pass urine for at least 1-2 hours prior to the procedure.

The patient lies supine on the examination table. The lower abdomen and suprapubic area is thoroughly cleaned with antiseptics. Suprapubic puncture of the urinary bladder is done using a 22 gauge needle about 2 cm above the pubic symphysis in the mid-line. A small amount of urine is drawn into the syringe to make sure that the needle has entered the bladder cavity. 37-74 MBq (1-2 mCi) of $^{99}Tc^{m}$ DTPA is injected in a volume of about 1 cc into the bladder and the needle is withdrawn. In children, a normal size (38 mm length) disposable needle is good enough to enter the urinary bladder. However, in adults, a large needle, preferably an intracath with a 45 mm long needle, is required. In a properly prepared patient with a reasonably full urinary bladder, it is possible to enter the urinary bladder without much problem. Care should always be taken not to inject any radioactivity into the bladder wall. After this the patient is placed before the gamma camera, and serial images of the urinary bladder in anterior projection are obtained at rest, every ten seconds for a period of 5-6 minutes. Following this, the patient stands with his back facing the gamma camera detector and passes urine without interruption into a container. While the patient is micturating, images of the urinary bladder and lower abdomen are obtained in frame mode (total frames: 120, time per frame: 1 second) using appropriate computer software. The total amount of urine passed is accurately measured.

Serial images of the urinary bladder are visually inspected frame by frame to see evidence of VUR. Sometimes contrast enhancement of the images may be essential for the detection of minor degrees of reflux. Following this, an appropriate frame or a combination of a few frames is selected to mark the regions of interest (RIO) by a computer light pen ( or any other suitable device). RIO's are selected over the urinary bladder, areas corresponding to the upper urinary tracts on both sides and background. Time activity curves are generated over these regions. This particular technique is based on certain assumptions, which are:

(a) concentration of radioactivity in the bladder is uniform at the time of study; and

(b) there is a linear correlation between external counting and radioactivity inside the bladder, while its contents are progressively decreasing. Based on these assumptions, the counts recorded during the study will be proportional to the volume(s).

From the relationship derived from the volume and radioactivity of the voided urine sample, it is possible to quantitate the bladder volumes - initial and residual, i.e. before and after the act of micturition, respectively. It is also possible to quantitate the urinary flow rate by processing the bladder activity clearance curve and calculating the maximum urine flow rate for a given bladder volume. There is of course the need to standardize the test, validate the results and define normal ranges for these parameters in the given population before the test results can be interpreted for clinical management of patients.

## 7. First-pass renal angiography

Radionuclide first-pass scintigraphy has become an established procedure after the advent of the gamma camera computer system and the most favoured radionuclide for this is $^{99}Tc^{m}$. Both qualitative and quantitative evaluation of organ perfusion are done with this procedure. In relation to the kidney, this technique has been applied in the diagnosis of patients with renal artery stenosis and renovascular hypertension, in the differential diagnosis of mass lesions of kidney, and in the evaluation of patients with renal trauma. But this technique has proved its usefulness most illustratively in the evaluation of renal transplant dysfunction, particularly to distinguish acute rejection from other causes of transplant dysfunction.

### Renal transplant perfusion index (RTPI)

RTPI is one of the quantitative indices derived from the first-pass renal scintigraphy study. Essentially, this parameter defines the ratio of blood flow to the kidney transplant and the artery that supplies blood to it. This index is expressed in many ways. The following is the technique used by the author to determine the RTPI.

The test is performed with the patient lying in supine position with the transplanted kidney under the field of view of the camera. The technique involves the intravenous bolus injection of 185-370 MBq (5-10 mCi) of $^{99}Tc^{m}$ DTPA. Immediately following the intravenous injection, rapid sequence dynamic images of the transplant are obtained in frame mode (in a total number of 127 frames) by using a histo-acquisition programme with variable time facility. For the first forty frames, the acquisition of data is done at a faster rate (time per frame: 1 second). After that the acquisition is done at a slower rate (time per frame: 16 seconds). This is done in order to have a good separation between the first-pass perfusion curve and the subsequent uptake function curve of the kidney (**Fig. 31.7**).

The sequential images are first examined frame by frame to assess qualitatively renal perfusion, renal cortical and collecting system morphology, and to select appropriate frame for marking the regions of interest (RIO). RIO's are selected over the transplant, external iliac artery, urinary bladder and background. As and when necessary, an RIO can also be selected over the ureter. All the RIO's are normalized prior to background correction. Corrected time activity histograms are generated from each RIO.

The transplant perfusion index is determined by taking into consideration the area under the normalized arterial and renal curves up to the peak of the arterial curve caused by the first passage of the radioactive bolus and is calculated by the following formula:

$$\text{Renal transplant perfusion index (RTPI)} = \frac{\text{Area under the arterial curve up to the peak}}{\text{Area under the renal curve up to the time of peak arrival of arterial curve}}$$

When the two areas are identical, the TPI has a value of unity. As relative blood flow through the kidney is reduced, the area under the perfusion phase of the renal curve becomes smaller, and the value of TPI increases. **(Fig. 31.8).**

**Fig. 31.8** shows diagrammatically the determination of RTPI. The RTPI has been shown to have a very discriminating value in the differential diagnosis between acute rejection and acute tubular necrosis, two common conditions affecting a renal transplant. **Fig. 31.9** illustrates this discriminating value of RTPI in 70 scintigraphic studies done in renal transplant recipients.

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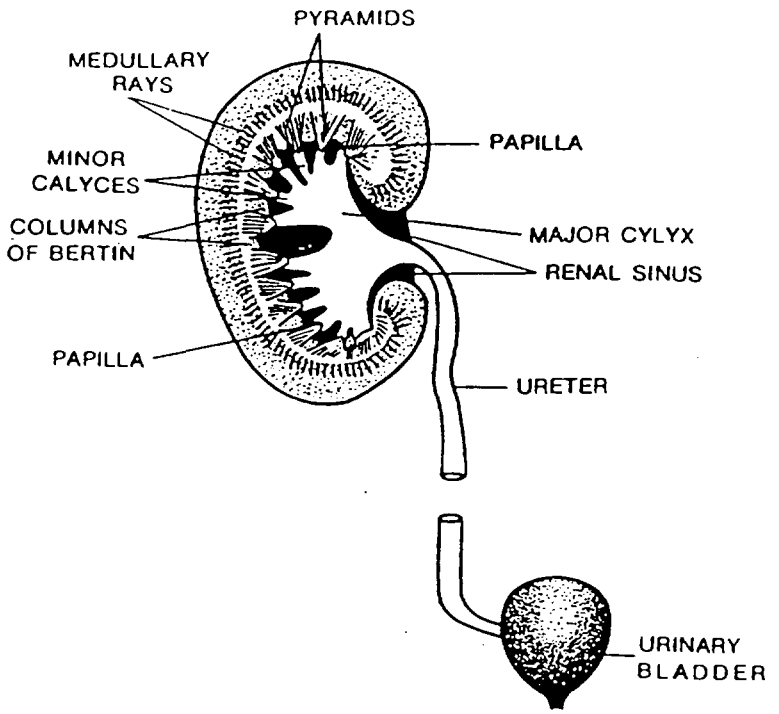


**Fig. 31.1** Gross anatomy of kidney and upper urinary tract.

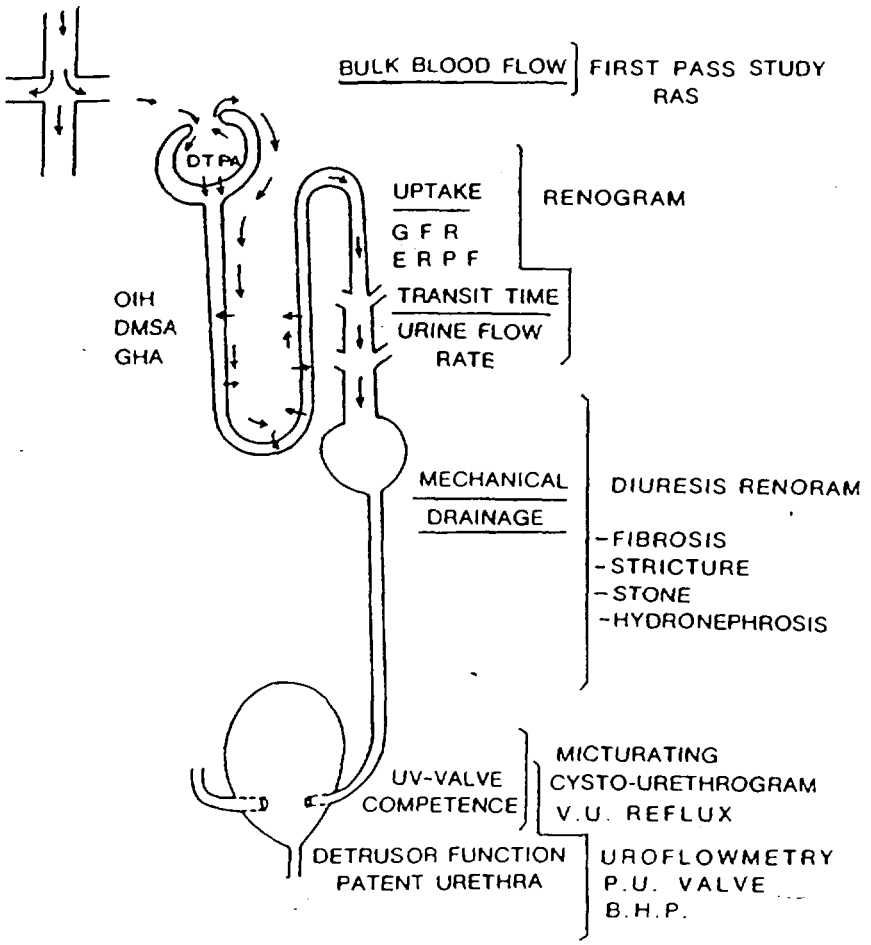


**Fig. 31.2** Functional anatomy of nephron. The radiopharmaceutical arrives at the nephron via renal artery (top left). It is handled by filtration and/or tubular secretion and passed into the lumen of collecting tubule. The physiological parameters and the related functional segment of nephron are indicated. The radionuclide investigations and their major indications are also mentioned.

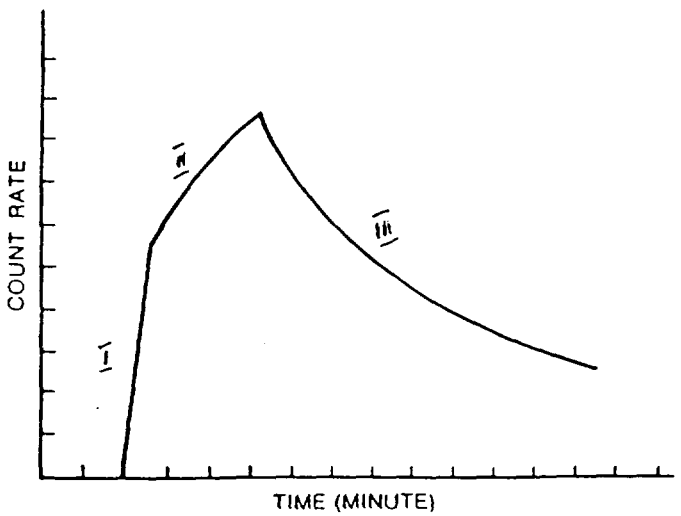


**Fig. 31.3** The normal renogram curve showing the classical three phases.

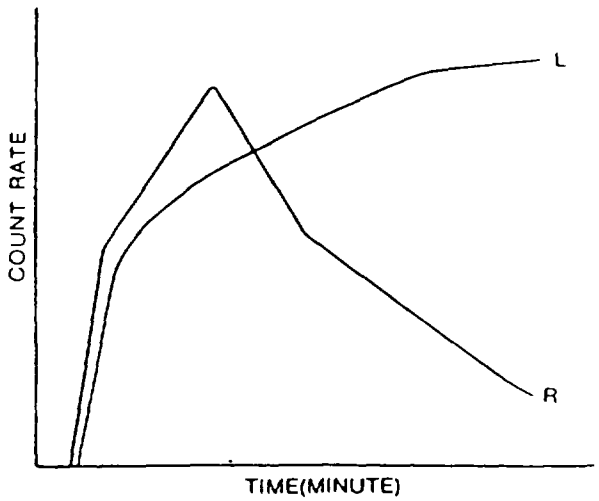


**Fig. 31.4** The renogram pattern in a patient with unilateral obstructive uropathy (LT side) showing an absent third phase.

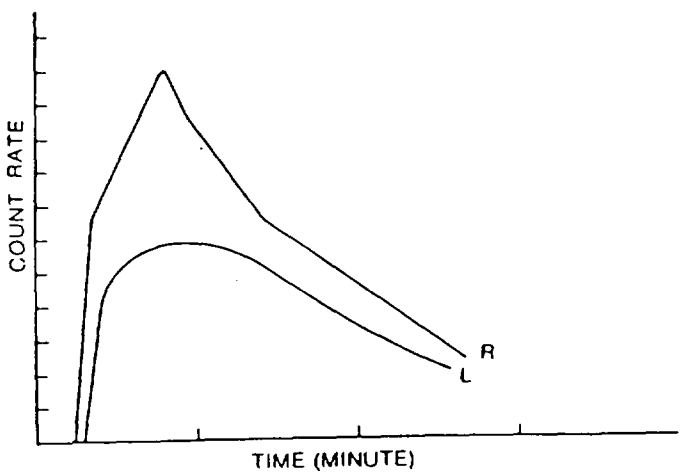


**Fig. 31.5** The renogram pattern in patient with left-sided parenchymal disease showing a flattened phase II and delayed peak due to compromised renal function, but no evidence of any obstruction to urine outflow.

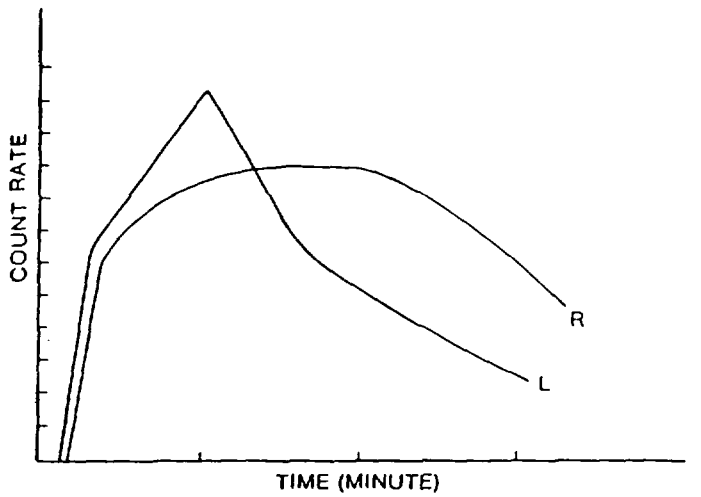


**Fig. 31.6** The renogram pattern in patient with unilateral (right side) renal artery stenosis showing flattened phase II, delayed peak and prolonged phase III.

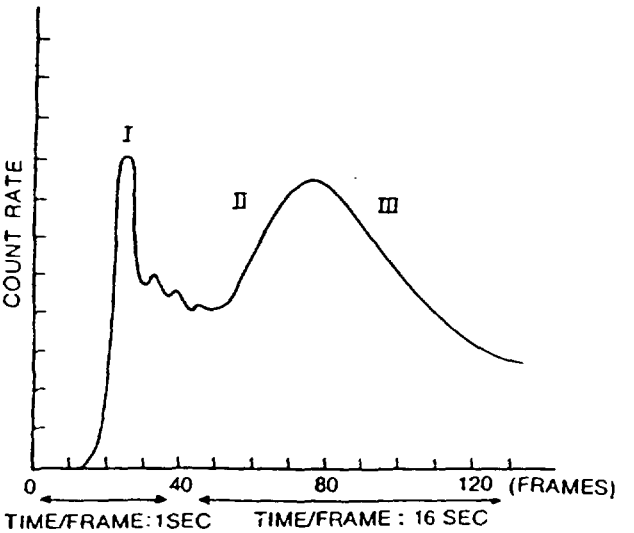


**Fig. 31.7** $^{99}Tc^{m}$ DTPA study using a gamma camera-computer system with variable time acquisition. Normal study. Note the separation between the first-pass perfusion curve (I) and the function curve (II and III)

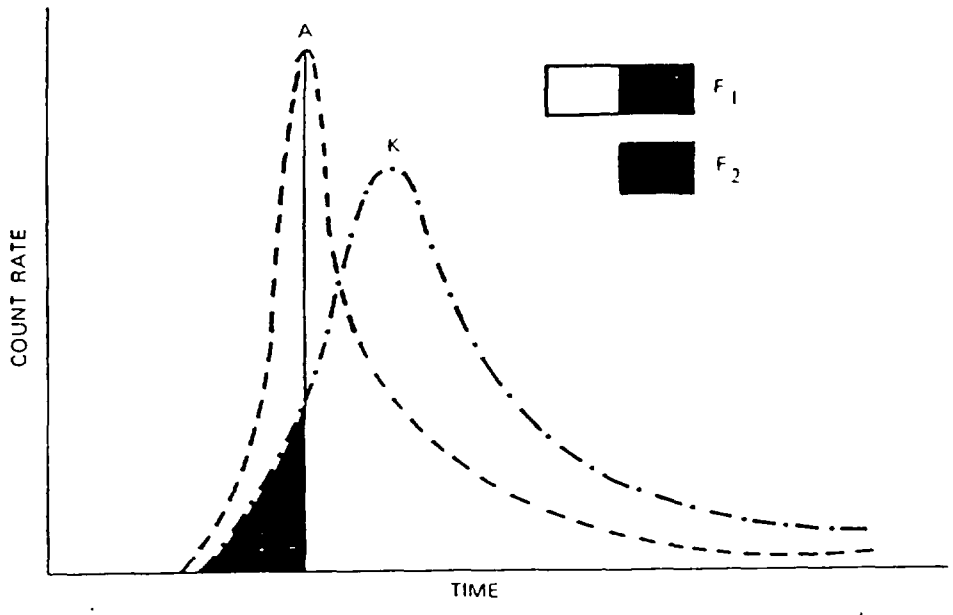


**Fig. 31.8** Determination of perfusion index from the first-pass time activity curves over the external iliac artery and the transplant RTPI = $F_1/F_2$.

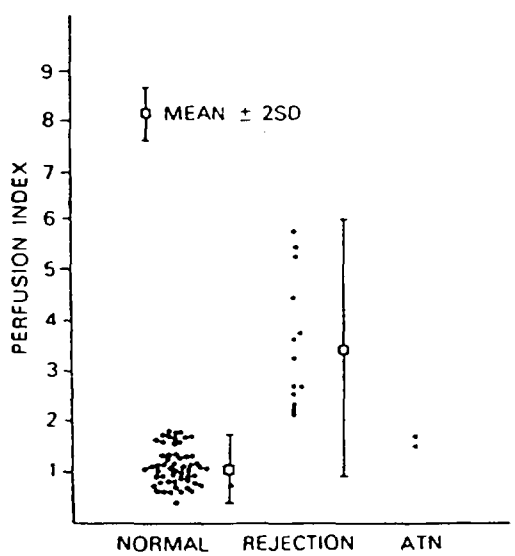


**Fig. 31.9** Perfusion index in normal, acute rejection, and acute tubular necrosis