Nuclear Medicine in Pediatric Urology and Nephrology

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Renal scintigraphy is a diagnostic procedure of choice or a complementary imaging modality in the work up of infants and children with urologic or nephrologic problems. New radiopharmaceuticals and techniques and expert interpretation provide unique renal parenchymal and collecting system functional and anatomical information, which helps in the diagnosis and follow up of congenital or acquired kidney disorders and the quantitation of renal function. Education of the user and the referring physician, further clinical experience, and comparative studies should help increase utilization of renal scintigraphy in the neonatal and pediatric age for the benefit of the patient and the better understanding of urologic and nephrologic disorders.

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Improved instrumentation and new radiopharmaceuticals and techniques have lead to increased use of scintigraphy in infants and children with urologic or nephrologic problems. Although other imaging modalities have, in general, better resolution, urinary tract scintigraphy has advantages in demonstration of regional function. Scintigraphy provides unique diagnostic information useful in both the initial evaluation and the follow-up of the patients with diseases of the renal parenchyma, collecting system, or lower urinary tract (*1*).

A thorough integration of the anatomical and functional information obtained by scintigraphy enables the experienced interpreter to go beyond generalities and to frequently advise the referring physician about the functional status and the specific diagnosis of a number of congenital and acquired renal disorders of infants or children. Renal scintigraphy is indicated as a screening test, as the diagnostic procedure of choice, or as a complementary imaging modality in many clinical presentations. Important decisions about further work-up, mode of therapy, duration of treatment, follow-up visits, and prognosis can be influenced by scintigraphy. Renal scintigraphy has a number of advantages in the pediatric patient (Table 1). The most important of these are that the studies are relatively nonoperator dependent and noninvasive with minimal risk and discomfort.

It is the purpose of this article to show characteristic features of renal scintigraphy, which serve to increase the specificity of the procedures. Appreciation and recognition of these by interpreters will amplify the usefulness of the modality in clinical practice to the benefit of patients.

RENAL SCINTIGRAPHY IN PEDIATRICS

RADIOPHARMACEUTICALS

Currently several technetium-99m-labeled (^{99m}Tc) complexes are in clinical use which are helpful in studying renal anatomy function (*2*).

Technetium-99 diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA), a glomerular filtration (GFR) agent, has been widely used for GFR measurements and for scintigraphic semiquantitative studies of renal blood flow and regional function including drainage. Anatomical information can also be obtained during the initial 10–20 min after injection.

Technetium-99m dimercaptosuccinic acid ([^{99m}Tc]DMSA) is an excellent imaging agent because ~40% of the dose accumulates in the tubular cells in 6 hr, providing excellent visualization of the cortices after the background activity clears (6–24 hr postinjection). DMSA is also partly cleared by glomerular filtration.

Technetium-99m glucoheptonate ([^{99m}Tc]GH) is a very useful radiopharmaceutical in clinical practice because it combines some features of DTPA and DMSA

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Table 1
Advantages of Pediatric Renal Scintigraphy

TECHNICALLY EASY
No preparation except hydration.
No sedation, but only immobilization.
Dressings, wounds, bowel gas, and tubes do not interfere.
Available at bedside (OR-ER).
Easy to perform following short term training.
Not operator-dependent after protocols are set.
ACCEPTABLE/AFFORDABLE
No reactions to radiopharmaceuticals.
Well acceptable, except venipuncture and catheterization.
Radiation exposure within or less than radiologic studies.
Cost in the lower range of imaging procedures.

scintigraphy. GH is mostly excreted by glomerular filtration and, like DTPA, is useful in the study of renal blood flow, glomerular function, and urinary drainage. About 10% of the injected dose of GH accumulates within the tubular cells in 6 hr like DMSA, thus enabling delayed scintigraphy of the cortices (3–6 hr post dose). GH, however, has the advantage of lower renal radiation compared with DMSA, thus allowing the use of higher doses which permit better flow-function-drainage studies. However, as it is excreted to some extent in the bowel, perplexing images may result when scanning occurs 24 hr postinjection, particularly if renal insufficiency exists.

Finally, Iodine-131 orthoiodohippurate ([^{131}I]HIP), is a very efficient tubular imaging and function agent since it is 80% cleared by tubular excretion, and only 20% by glomerular filtration. HIP is an essential renal plasma flow agent (ERPF) (*3*). For renographic studies, small dosages of [^{131}I]HIP are used although the long half-life of ^{131}I (8 days) and its beta emission and energetic gamma rays (364 keV) make it less desirable than ^{123}I from the standpoint of radiation dosimetry and collimation. Iodine-131 hippurate has a long shelf life, is much less expensive, and can be used in dual imaging procedures following or preceding ^{99m}Tc agents.

METHODS

Renal scintigraphy is performed in posterior projection sequentially for 20–30 min after injection of the radiopharmaceutical of choice and, when indicated, delayed static images may complement the study. With DTPA or GH, sequential imaging starts as 1-min flow phase (1–2 sec images) and continues as 20–30-min function phase (usually 30 sec images in computer and 2-min images on radiographic film or polaroid). With HIP, only the function phase (renography) is performed. Computer generated time-activity graphs (renograms) of the total kidney or its parts can be analyzed semiquantitatively (slopes, peak-times, half-times, deconvolution analysis, residual cortical activity, etc.), and frequently amplify the ability of the observer to detect subtle changes. Delayed scintigrams (posterior and oblique, high resolution, 300–500 thousand count views) at 3–6 hr (GH) or 6–24 hr (DMSA) are especially useful for the detection of focal cortical lesions or the determination of the level of obstruction.

The patient should be supine or seated if possible, well hydrated, calm and comfortable in a warm environment with the parent present. An indwelling needle should be gently inserted into a peripheral vein before injection and the absence of extravasation should be verified. Sedation may be administered if needed, and the infant or child should be carefully immobilized to assure optimal results. Equipment must be in excellent condition and operate flawlessly for pediatric patients. DTPA and GH are injected intravenously in a dose of 200 μCi/kg, and DMSA 100 μCi/kg (minimal ^{99m}Tc dose, 1 and 0.5 mCi, respectively). Iodine-131-HIP is injected intravenously in a dose of 20 μCi/kg (minimum 50 μCi).

The Normal Scintigram

The interpretation of the scintigrams should be based on the appearance of: 1) the renal parenchymal and collecting system activity; and 2) the abdominal background activity. Characteristic features of normal renal scintigraphy with technetium complexes are shown in Figure 1A-B.

Flow studies. In the infant, these studies may be useful in some clinical situations like acute tubular necrosis (ATN); they are more informative in the child because of size and resolution, but require the administration of a good bolus injection. Renal activity should be orthotopic, symmetric, simultaneous in the two kidneys and of equal intensity with the aortic activity.

Parenchymal accumulation and excretion, ureteral and bladder appearance. After the bolus' first pass, activity increases in the kidney for 2–5 min. Peak activity of the cortex usually occurs between 2 and 3 min. The familiar bean-shaped normal kidney appears on the scintigrams orthotopically, medially and caudally to the spleen on the left, and caudally to the liver on the right and with the variable size according to age. The intrarenal collecting system usually appears between 2–4 min. Ureteral visualization is not common in normal well hydrated patients. The ureters may become visible intermittently between 3–20 min. Continuous visualization of the ureters, especially with delay, may be due to obstruction, compression, megaureter, or dehydration. Bladder activity usually becomes visible 3–10 min after injection; increasing in intensive focal activity in the pelvis appearing immediately after injection, before 2–3 min, usually indicates pelvic ectopia. Peak renal (including collecting system) activity occurs 3–5 min after injection. Cortical activity declines

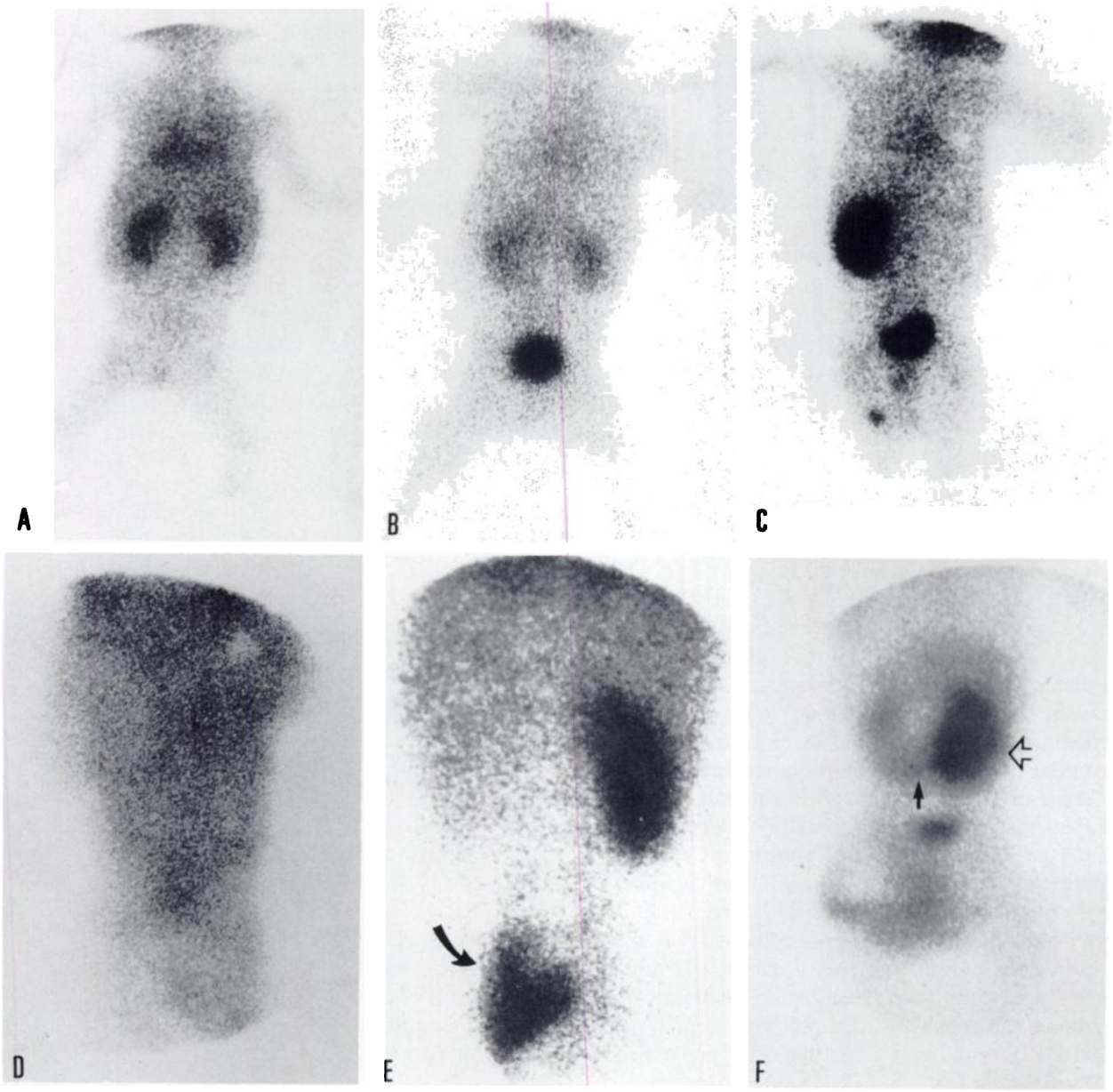

FIGURE 1
Technetium-99mGH scintigrams of normal kidneys (A-B) in a newborn, 2 min (A) and 20 min (B) after injection. Agenesis in newborns, unilateral (C) and bilateral (D). Pelvic ectopia (E) in a child and a horse shoe kidney (F) in an infant. In all cases, the abdominal background is normal (compare with Fig. 2–4). Renal activity is seen early (1–3 min) orthotopically (bilateral in A, unilateral in C and E) or ectopically (E, arrow). In agenesis renal activity is absent (unilaterally in C, bilaterally in D). In agenesis and ectopia there is normal background activity in the renal bed (compare with photopenic defects in cystic disease, obstruction, reflux (Fig. 2–4)). Bladder activity appears after 3–5 min (B,C,F), unless there is bilateral agenesis (D), bilateral obstruction (see Fig. 3), renal failure or dehydration. The horseshoe kidney (F) is characterized by caudally converging longitudinal axes of the kidneys and (usually in anterior view) by visualization of a functioning bridge of renal tissue connecting the lower poles of the kidneys (small arrow). In the case presented here there is also a partial obstruction (enlargement and retention of activity) of the right moiety (open arrow), a common finding in this anomaly. The patients were referred to the NM because of infection, except patient (D) who had anuria and renal failure.

after peaking and practically disappears at 20–30 min with DTPA; after a peaking and initial decline cortical activity stabilizes and slowly increases with DMSA and GH. At 20–30 min post-dose, in a well hydrated patient, the collecting system normally empties with only a slight amount of tracer visible after that with ^{99m}Tc complexes. Postural pooling can be ruled out by obtaining a post-voiding or post-upright image. Renal insufficiency and dehydration delay the time sequence of concentration and excretion.

Normal abdominal background. The spleen and liver blood pools are usually visible in the parenchymal images the first few minutes after injection, but with much lower and decreasing intensity than the normal kidneys. A full urinary bladder may appear as a photon deficient region before excreted activity reaches that organ. A full stomach also produces a photon deficient region superiorly and laterally to the left kidney. The rest of the abdomen usually shows uniform background activity in the normal state. Background defects (photon deficient areas), other than those mentioned above, usually signify some kind of pathology related to the kidneys. Rarely, they may be the result of severe intestinal dilatation, or an intraperitoneal cyst or ischemic lesion.

Hepatic, gall bladder, and intestinal excreted activity may be visible on delayed (6–24 hr) images with GH, particularly if renal insufficiency exists. Intestinal activity may at times mimic ureteral activity.

Delayed images. Delayed images with GH or DMSA show mainly renal cortical activity. Kidney images should resemble the shape of a bean, but the pelvis and calyces may appear as regions of decreased activity, depending upon the size of the kidneys and the resolution of the camera. The kidney margins are usually smooth, but lobulation can be present as a normal variation. Visualization of the collecting system on delayed images is suggestive of obstruction or reflux. However, renal insufficiency or dehydration may result in delayed collecting system visualization even without anatomical abnormalities. Indentation of the upper lateral margin of the left kidney by the spleen is a common finding and should not be confused with a renal lesion.

Hippuran scintigraphy. This is indicated for the study of obstructive uropathy, renal failure, and renovascular and diffuse parenchymal diseases. The normal study is characterized by rapid accumulation of activity in the kidney for the first few minutes after injection. Renal activity peaks 3–5 min post-dose, appears in the bladder at 3–5 min, and is exclusively in the bladder 10–20 min later with only traces remaining in the kidneys after that.

Renogram. The renograms from the two kidneys should be nearly identical in shape and slopes. Slight differences in height may be due to normal variation in kidney size or position, to patient positioning, or region of interest assigning. Following the arrival of the HIP bolus (not visible in 30-sec sequential histograms) renal activity rapidly increases, peaks and then declines because of a drop in blood-pool activity (renal accumulation and extravascular distribution) and excretion by the kidney. From then on, hippurate activity falls precipitously. At 20 min, hippurate renal activity is normally <20% of the peak. The cortical graphs are more steep and peak earlier.

Renal II insufficiency. An advantage of scintigraphy over excretory urography is the ability to visualize kidneys scintigraphically in renal insufficiency. Peak time delay, lower intensity of the urinary tract activity, and persistent high background activity are characteristic of renal insufficiency. The contribution of scintigraphy in the workup of patients with renal insufficiency or failure is discussed later.

Total Renal Function

Radioisotope studies can provide renal clearance measurements with a single injection and without urine collection (*4*). Multiple blood sampling methods are based on Sapirstein's initial work as simplified by others. Single blood sampling methods are based on empiric observations that plasma concentration of an injected substance at a specific time reflects its clearance (distribution volumes and regression analysis). Finally, methods based on quantitation of renal uptake by scintigraphy without blood sampling or combinations, provide useful information according to some authors (*4*). GFR and ERPF can be measured by these methods, and the filtration fraction (FF = GFR/ERPF) can then be calculated.

Split Renal Function

The function of one kidney as compared to the other (split renal function) is needed information when nephrectomy or corrective intervention is contemplated. It can be calculated easily in any nuclear medicine laboratory with a camera and a minicomputer without the necessity for collecting urine from each ureter. There are two techniques: (a) quantitation of radioactivity present in the kidneys the first 2–3 min after injection and before activity enters the ureters (*5*); (b) quantitation of cortical activity after the collecting systems are emptied (usually at 24 hr) (*6*).

The first approach can be applied using any radiopharmaceutical which is excreted by the kidneys. Background correction is required, therefore, agents with greater renal clearance are better suited. HIP (^{123}I or ^{131}I) is the best; DTPA and GH are less accurate than HIP in the presence of renal failure. This approach is rapid and can be employed in the presence of obstructive uropathy.

The second approach requires the use of radiopharmaceuticals with cortical fixation such as DMSA. At 24 hr, there is little interference from background radioactivity but obstructive uropathy may invalidate the results. The greatest disadvantage is the need for a return visit by the patient on the following day.

The split renal function computed with any of the above methods or radiopharmaceuticals merely represents function at the time of the study and not renal function reserves.

By combining clearance and split renal function measurements, the actual function of each kidney in

terms of individual clearance (ml/min) can be calculated.

INDICATIONS

A number of indications exists for renal scintigraphy in the workup of the pediatric patient (Table 2). The following sections identify those that are most important.

Congenital Urinary Tract Anomalies

Congenital urinary tract anomalies (CUTA) can be unilateral or bilateral. Unilateral CUTA may be recognized as asymptomatic abdominal masses by ultrasonography, prenatally and postnatally, or by clinical examination of the newborn. They may be complicated by infection or hypertension and diagnosed in the workup of these complications in the infant, the child, or even the adult; they may be uncovered in the process of investigating a patient with other congenital malformation and, finally, in a significant percentage, they may escape recognition both during childhood and adulthood. Bilateral CUTA, however, in addition to the above, may manifest themselves as acute or chronic renal failure in the neonate, the child or the adult, depending on the specific malformation. Thus, the presentation of a patient with congenital renal disease varies from asymptomatic to renal failure. The most common presentation, however, is that of abdominal masses in the newborn and urinary tract infection in the infant and the child. In fact, CUTA is the most common cause of abdominal masses in the newborn.

TABLE 2
Indications for Renal Scintigraphy

Neonate and Infant	Child and Adolescent
1. Abdominal masses	1. Follow-up of patients with congenital renal disease with or without corrective surgery
2. Oliguria, anuria (renal insufficiency, failure)	2. Urinary tract infection workup
3. Hypertension	3. Hypertension
4. Urinary tract infection	4. Suspicion of renal vein thrombosis (nephrotic syndrome)
5. Hematuria	5. Workup and follow-up of patients with nephrologic problems
6. Search for congenital anomalies	6. Acute renal emergencies (renal failure)
7. Myelomeningocele-Prune Belly Syndrome	7. Abdominal masses
8. Trauma	8. Hematuria
9. Perinatal ultrasonographic findings	9. Trauma space-occupying lesions

The complex evolution of the kidney provides adequate potential for the development of a variety of congenital problems of the kidneys and of the collecting system (*7*) (Table 3).

The specific diagnosis of the congenital disorder is usually made with a combination of imaging procedures (scintigraphy, ultrasonography, pyelography, cystography, and urethrography) not infrequently requires endoscopy and retrograde imaging, and sometimes it is only comfirmed at surgery. Scintigraphy can depict regional cortical function anywhere in the abdomen, can differentiate obstruction from cysts and reflux nephropathy, and can indicate the level of the obstruction, advantages that help provide diagnostic information as to the specific type and the functional significance of the congenital anomaly (*8–12*). Figures 1 through 4 depict the most common types of congenital anomalies of the urinary tract with specific features seen on renal scintigraphy and the differential diagnosis.

Scintigraphy and ultrasonography are complementary modalities (*13*). In our experience, scintigraphy has been found to be more specific than ultrasonography (*14*). Agenesis versus ectopia, multicystic kidney

TABLE 3
Common Congenital Anomalies of the Urinary Tract

Anomalies of the kidneys

1. Anomalies of renal content
   (a) agenesis
   (b) hypoplasia
   (c) oligomeganephronia
2. Renal cystic disorders
   (a) multicystic dysplastic kidney (and other dysplasias)
   (b) polycystic kidneys (infantile-adult)
   (c) renal cysts (simple, pyelogenic, and multilocular)
   (d) renal medullary cystic disorders (medullary sponge kidney, etc.)
3. Anomalies of position, form, or orientation
   (a) ectopic kidneys
   (b) horseshoe and fused kidneys
   (c) malrotation of the kidney
   (d) duplications(?)

Anomalies of the draining system

1. Without obstruction (megacalyces—diverticula, etc.)
2. Obstructive
   (a) ureteropelvic junction obstruction (proximal)
   (b) ureterovesical junction obstruction (distal)
   (c) ectopic ureter with obstruction (distal)
   (d) bladder outlet obstruction
   (e) posterior urethral valves
3. Neuromuscular
   (a) neurogenic (neuropathic) bladder
   (b) idiopathic megaureter
4. Vesicoureteral reflux
   (a) primary (ureterovesical junction)
   (b) secondary (bladder outlet obstruction-valves)

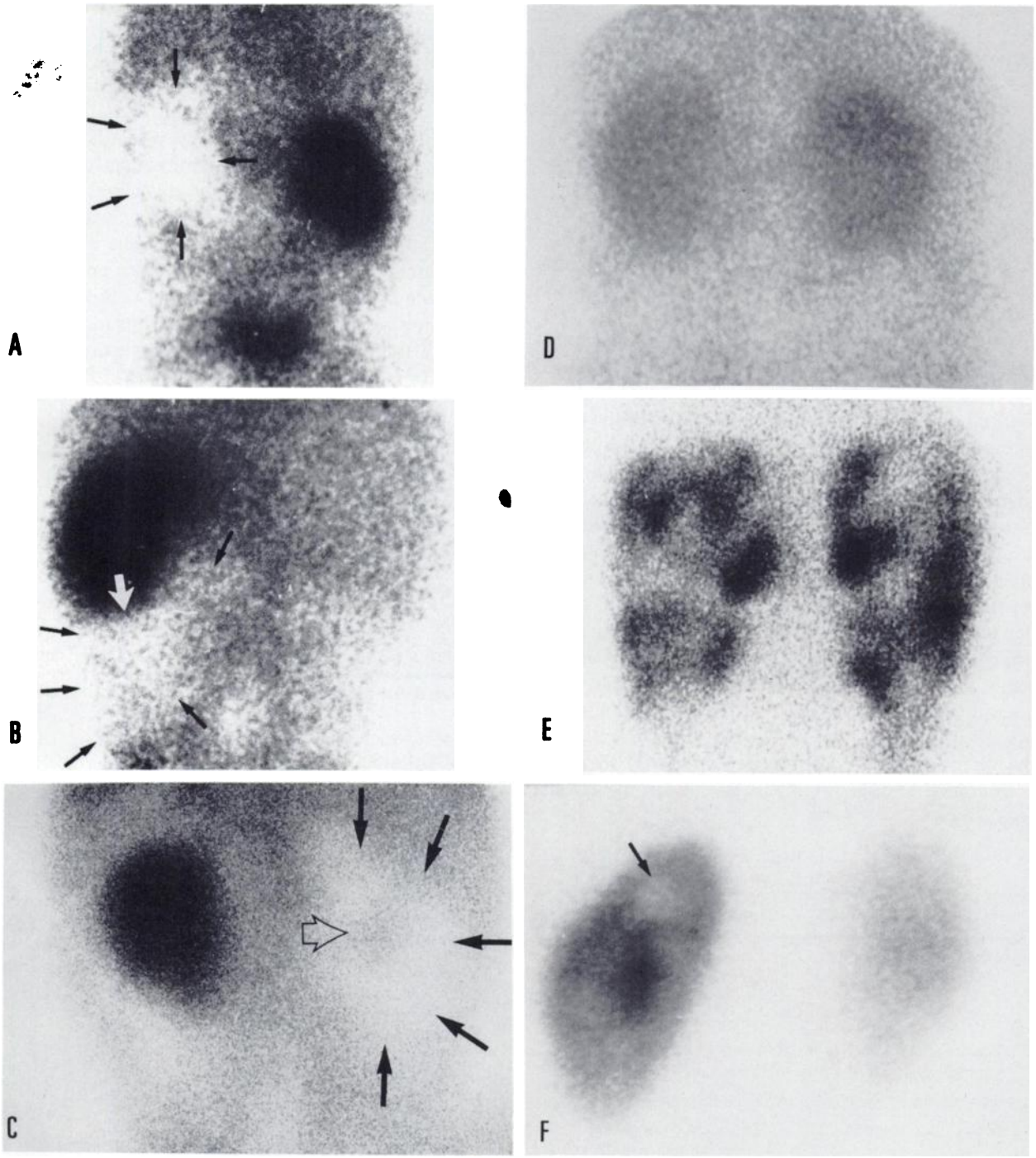

FIGURE 2
Technetium-99mGH scintigrams in renal cystic disorders: Multicystic kidney (A-C) is characterized by a defect in the background activity (arrows) orthotopically (A,C) or ectopically (B) and by either total lack of functional activity (A,B) or (C) a central or medial functioning (?) region (open arrow) surrounded by the photopenic defect (arrows) (compare with agenesis, simple ectopia (Fig. 1), hydronephrosis (Fig. 3), reflux nephropathy (Fig. 4). Polycystic kidney disease infantile type (D) in a child with renal insufficiency; the small cysts cannot be resolved and only enlargement of the kidneys and decreased function were present. Polycystic kidney disease adult type (E) in a young adult investigated for palpable abdominal masses; the functioning parenchyma is displaced by multiple nonfunctioning cysts and there is no obstruction. A simple cyst (arrow) on a delayed oblique view (F) in a patient with hematuria. Patients with cystic renal disorders may also be investigated currently because of perinatal ultrasonographic findings.

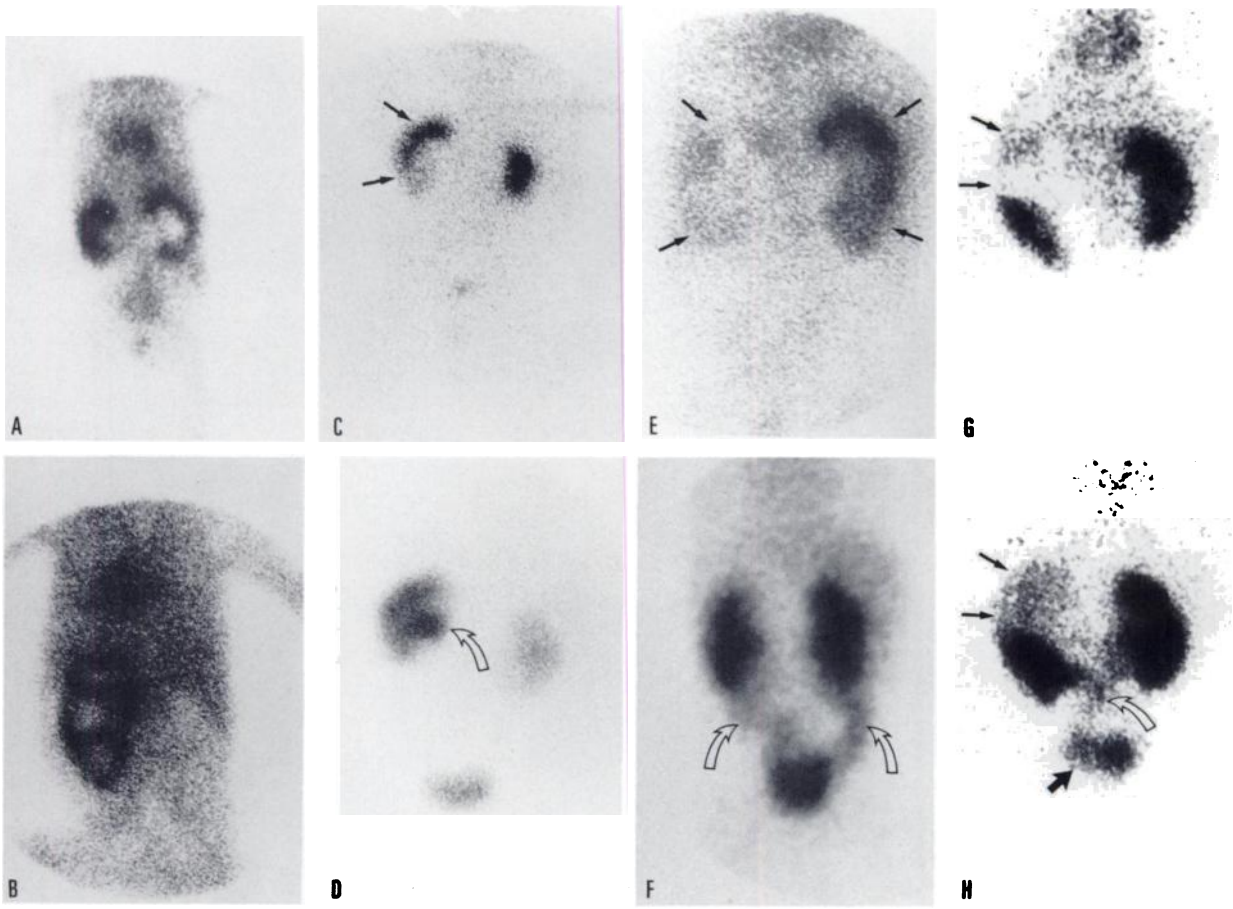

FIGURE 3
Technetium-99mGH scintigrams in obstructive uropathy: Hydronephrosis is characterized on the early pictures (2–10 min) by a rim of functioning parenchyma surrounding a photopenic collecting system (newborns, A,C,E), or photopenic dilated calyces (Children, B) (Compare with Fig. 1 ectopia, agenesis, Fig. 2 cystic disorders and Fig. 4, reflux nephropathy). The level of obstruction can be identified on delayed (4–6 hr) images (D,F). A ureteropelvic junction obstruction (UPJO, partial) is characterized by (C) hydronephrosis (arrows) and (D) pelvic retention (arrow) without ureteral visualization. A ureterovesical junction obstruction (UVJO, partial) shows (E) hydronephrosis (arrows) and (F) delayed ureteral visualization (arrows). A renal duplication with ectopic ureteral insertion into the bladder will show (G) partial (upper/medial) hydronephrosis (arrows), and (H) delayed ureteral visualization (open arrow) and, frequently, a bladder asymmetry due to the effect of the ureterocele (solid arrow). Bilateral UVJO should be differentiated from obstruction due to bladder hypertrophy or outlet obstruction and also from obstruction due to posterior urethral valves; scintigraphy with a bladder catheter in place can differentiate bilateral UVJO from other causes. Patients with obstructive uropathy are usually evaluated for UTI, abdominal masses or perinatal ultrasonographic findings.

versus severe obstruction, and proximal versus distal obstruction appear more readily with scintigraphy. It should be mentioned that recent experience in this, and other institutions, indicated that mild to moderate dilatations of the collecting system found on ultrasound perinatally may sometimes represent extreme variation of the normal. They are not associated with obstruction and they automatically resolve; GH scintigraphy and, if needed, diuretic renography are necessary to establish or rule out obstruction in these cases.

Intravenous pyelography is now performed only occasionally for the workup of the infant with urinary tract problems having been replaced largely by scintigraphy and ultrasonography. Finally, congenital anomalies have to be differentiated from common acquired renal diseases, parenchymal (ATN, etc.), and vascular (Fig. 5), traumatic lesions and inflammatory diseases (Fig. 6), and from the rare instances of renal tumors (Fig. 6).

Urinary Tract Infection

Renal scintigraphy and nuclear cystography are the most sensitive tests for the work-up of the children with urinary tract infection (UTI).

Acute pyelonephritis, acute bacterial nephritis (focal, multifocal, and diffuse), lobar nephronia and renal abscess are different forms of upper urinary tract (renal) infection, which need to be diagnosed and treated vigorously to prevent serious consequences, ranging from scarring to bacteremia. If renal involvement is excluded,

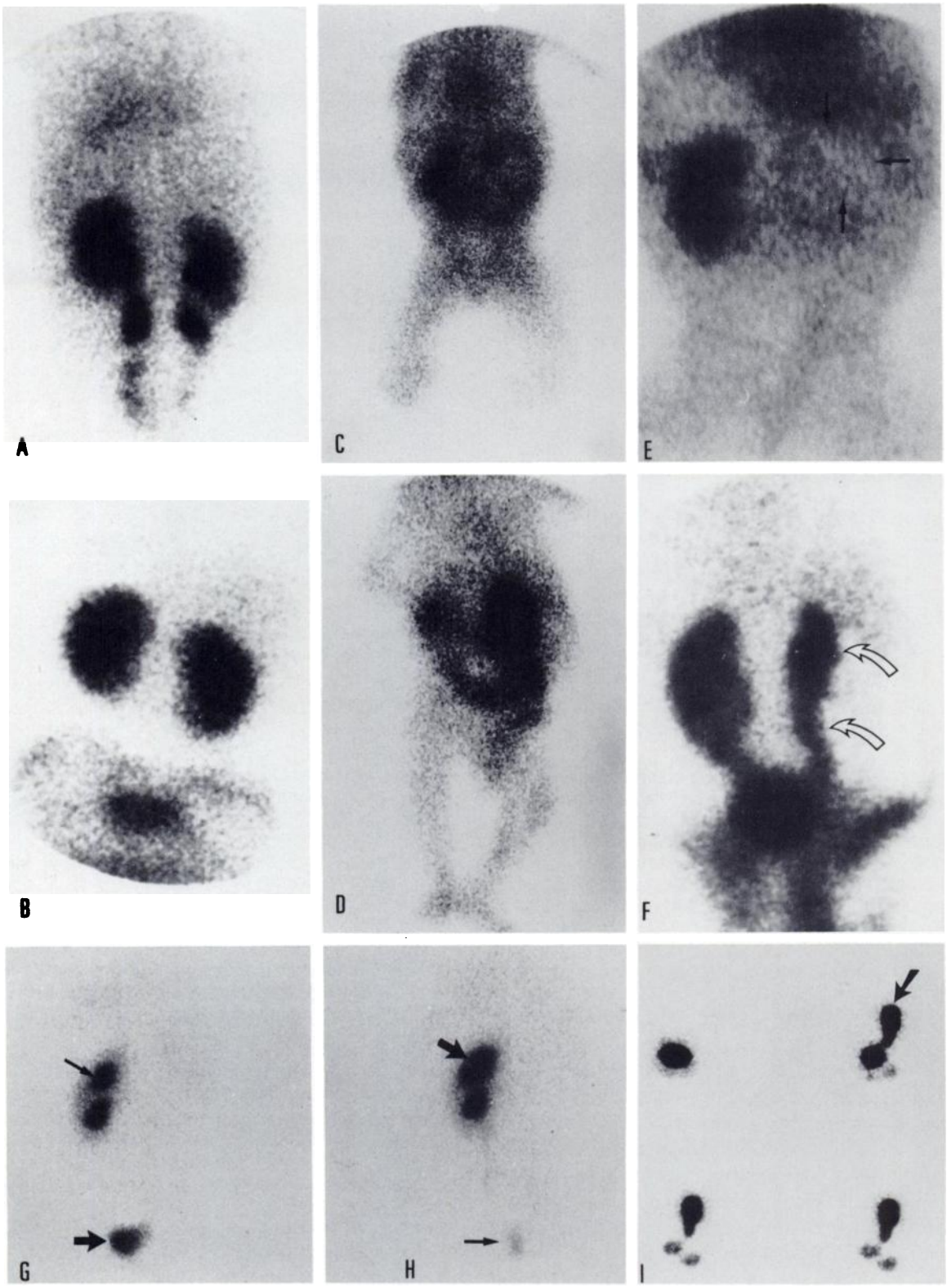

FIGURE 4
Technetium-99mGH scintigrams in patients with anomalies of the draining system: Neuromuscular disorders (A,B), posterior urethral valves (C,D) and reflux nephropathy (E-H). Persistent (5–20 min) ureteral activity (A), but normal delayed images (B) and normal diuretic renography (not shown) characterize neurogenic (neuropathic) uropathy, usually in patients with myelomeningocele. Posterior urethral valves (C,D) produce images showing distal obstruction (see Fig. 3). Vesicoureteral Reflux, if mild, may not damage the kidney, if moderate, may induce hydronephrosis, but if massive, may destroy renal parenchyma. The kidney then appears on early (1–10 min) images (E) as a small (compared to the large multicystic kidney) photon deficient region (arrows). When later (10–20 min), the patient empties the bladder (F), or on delayed images it usually fills (arrow) with bladder activity, derived from the other kidney. Vesicoureteral reflux can also be observed on GH scintigraphy as a backward flow of activity (G,H—reflux from bladder into the upper moiety of a fused ectopia). Reflux (arrow) can be diagnosed with a higher sensitivity by retrograde studies (I).

oral antibiotic treatment of urinary tract infections is usually effective.

Renal scintigraphy with GH or DMSA (delayed imaging) is invaluable for the diagnosis of acute unifocal or multifocal renal infection (*15*) (Fig. 6) and can also indicate (early phase of GH study) the specific underlying disorder in cases where infection complicates a congenital renal anomaly.

Scintigraphy is more sensitive than ultrasonography (US) and both are more sensitive than pyelography (IVP) (*16–17*). Computed tomography (CT) is more sensitive than US and IVP, but not compared as yet with scintigraphy. Infection induces focal defects on scintigraphy. Since the method is sensitive, but not specific, ultrasonography is required to rule out other etiologies. Ultrasonography is normal or shows slight changes in infection, but can clearly show scars, cysts, and tumors.

Vesicoureteral reflux (VUR), the second major predisposing factor of UTI, can be diagnosed and quantitated best with a retrograde radioisotopic study (Fig. 4). Gallium scintigraphy provides positive images of infection and may be indicated when active UTI is questioned.

Renovascular Disorders

Renal vein thrombosis (RVT), more common in the past when catheterization of the umbilical vein in the neonate was practiced, still remains a frequent complication in the child with nephrotic syndrome (*18*). Features of the diagnosis with renal scintigraphy are shown in Figure 5. RVT is catastrophic for the kidney of the infant, but in the child collateral veins and, later, recanalization of the thrombus's may permit return of renal function (*18*).

Renal artery stenosis (RAS) (congenital or acquired) or renal ischemia from aortic thrombus, (following complications of umbilical artery catheterization) can be the cause of renovascular hypertension (RVH) (Fig. 5). While baseline scintigraphy is sometimes abnormal, depicting decreased function of the stenotic kidney or infarcts in branch renal artery occlusions, frequently renin-angiotensin compensation renders baseline scintigraphy normal. It is then that pharmacologic intervention with captopril (a converting enzyme inhibitor) can temporarily decompensate renal function, by drastically decreasing GFR, thus inducing decreased DTPA or GH accretion or prolonged Hippuran retention in the cortex of the kidney. These findings after captopril treatment are characteristic of RAS, partial arterial obstruction or renal ischemia from aortic causes (*19*). Captopril is used to treat hypertension, and in patients with RVH from bilateral RAS or renal ischemia from aortic thrombus and in patients with a single functioning kidney with RAS, renal failure may be developed if the drug is continued. Single dose captopril scintigraphy may predict this complication by showing the temporary effect of the drug on renal function, thus providing a safety test for the treatment of hypertension with converting enzyme inhibitors (Sfakianakis G N, Damoulaki-Sfakianakis E, Zilleruelo G, et al. *Biol Neonate: submitted for publication.)*

Trauma and Space-Occupying Lesions

Scintigraphy with GH (or DMSA) is sensitive in diagnosing renal parenchymal and collecting system trauma (*20*). In the emergency situation, however, intravenous pyelography (IVP), or CT are usually applied for the investigation of the patient with UT trauma. While IVP is used traditionally, CT has the advantages of a better resolution, the three-dimensional presentation and the additional information about the spaces around the kidneys and the other organs and tissues of the abdomen. Thus, if the patient is to be transferred from the emergency room (ER) for further studies, CT is the method of choice. Urinary tract trauma may be seen sporadically in the nuclear medicine laboratory in neonates with trauma at birth investigated for congenital renal diseases or renal failure, in the child with occult trauma (e.g., child abuse) investigated for renal failure, or when IVP or CT are apparently normal in the presence of hematuria (Fig. 6). Iatrogenic urine leaks in patients postoperatively, or urinomas complicating renal transplants can best be studied with scintigraphy. Characteristic findings in different types of GU trauma are outlined in Figure 6.

Patients with space-occupying lesions (SOL) are usually investigated with IVP, US, or CT. US and CT provide information about the nature of SOL (cyst or tumor) and the extent of the lesion outside the contour of the kidney, as well as involvement of adjacent tissues, vessels, organs, etc. Renal scintigraphy with GH or DMSA can recognize most of the lesions as focal defects of the renal cortex (Fig. 6) and can frequently differentiate tumors from cysts based on the presence or lack of flow activity. SOL can be found fortuitously in patients undergoing scintigraphy for other causes. When, however, the other imaging modalities cannot differentiate with certainty between a tumor and a fetal lobulation or column of Bertini, scintigraphy is the method of choice. It should be noted that cortical defects found in scintigraphy are not specific because they can be the result of tumors or cysts (Figs. 2 and 6), trauma (Fig. 6), infarction and infection (Fig. 6), scars (Fig. 6), compressions by extrinsic organs or lesions, or even focal interstitial nephritis. The findings on renal scintigraphy should be interpreted within the context of the clinical presentation of the patient and with the help of other imaging modalities (e.g., ultrasonography).

Renal Insufficiency and Failure

Renal scintigraphy may provide diagnostic information about congenital and acquired diseases in patients

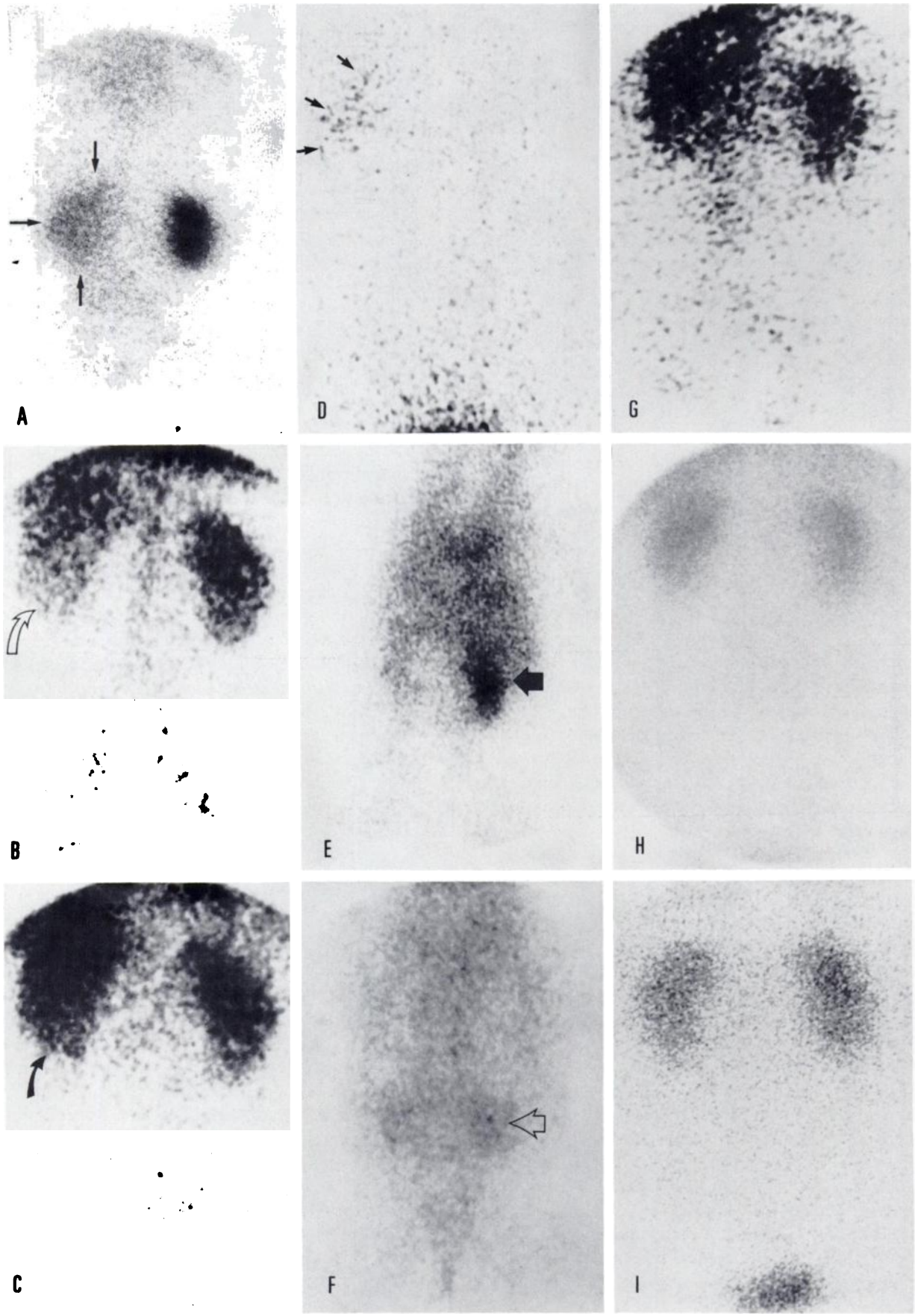

FIGURE 5
Scintigraphy in renovascular disease: Acute renal vein thrombosis (RVT, A) in a newborn infant manifested as a large kidney (arrows) with decreased function but no obstruction ([^{99m}Tc]DTPA). Old RVT (B,C) in a child with nephrotic syndrome (after recanalization of the vein) appearing on Tc-GH scintigraphy as delayed flow (open arrow) and congestion

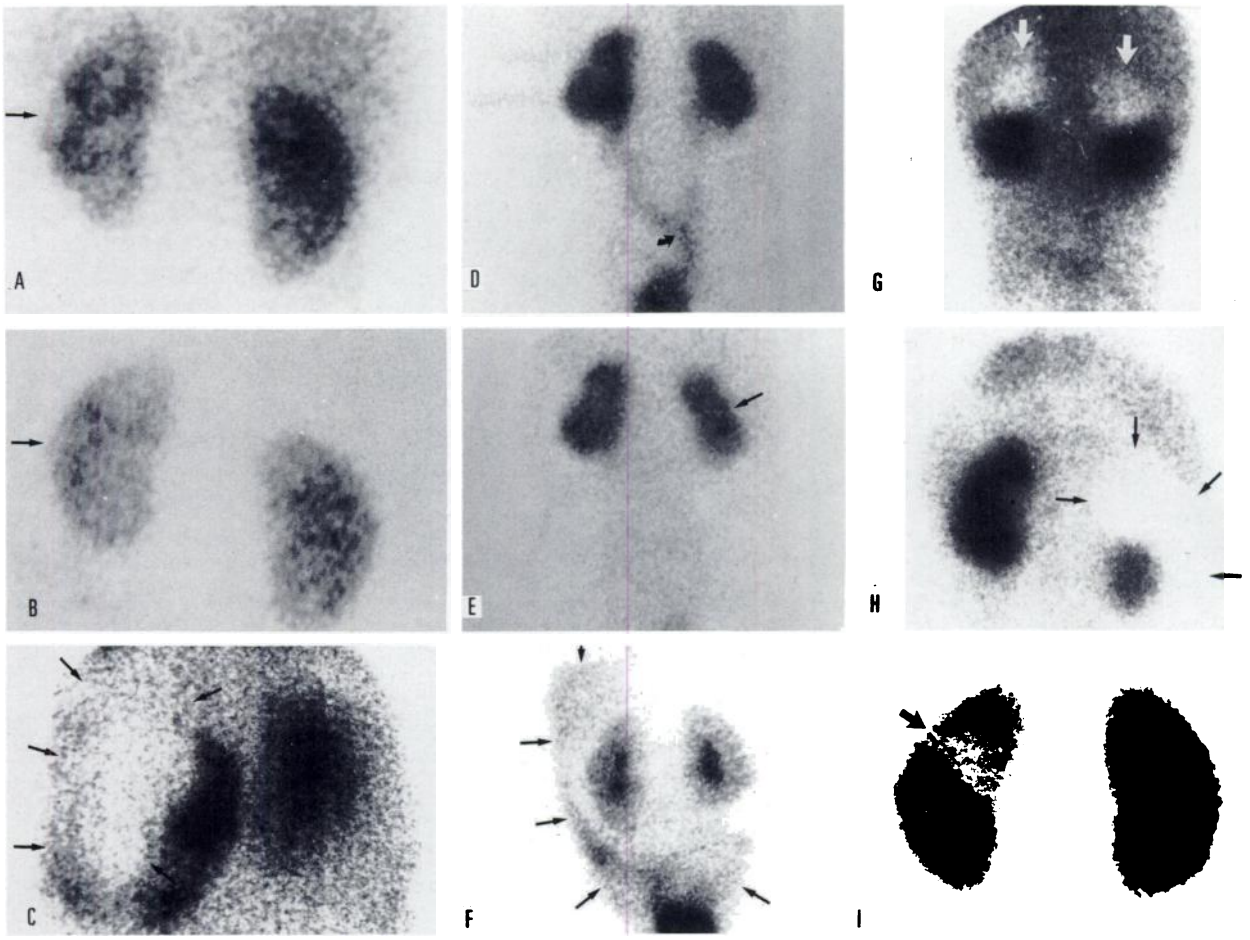

FIGURE 6

Tc-99m-GH scintigrams in pyelonephritis (A,B,D,E), renal trauma (F-I) and tumors (C). Acute focal pyelonephritis is manifested (A) as a focal defect on 4-hr [^{99m}Tc]GH magnified images (arrow) in a 4-yr-old boy; resolution of the lesion (B) is shown on follow up study (arrow). Focal defects (C-E) on scintigraphy could be due to space occupying lesions (C, Wilm's tumor) or scars (D,E, early and late images in a patient with scars and uretero-ureteral anastomosis). Ultrasonography can differentiate these lesions. Trauma (F-I) can induce collecting system rupture and uroperitoneum (F, ureteral rupture, child abuse), bilateral adrenal hematomas (G, newborn of a diabetic mother with abdominal masses), perinephric hematoma (H, child after automobile accident), renal fracture or avulsion, or renal contusion (I, adolescent after flank trauma, hematuria, and normal IVP).

with compromised renal function (*21*). Renal failure (RF) in the infant or the child can be caused by a variety of prerenal, intrinsic or post-renal causes, congenital or acquired. It can be the end stage of chronic renal disease or it can be acute failure. Imaging is needed in patients with renal failure to exclude correctable pathology and to confirm clinical suspicions. IVP is usually not informative and it may deteriorate renal function due to the osmotic effect of the contrast media. Ultrasonography may show renal size and collecting system size or SOL, but the lack of functional information is a disadvantage.

The most informative scintigraphic approach is to perform a triple-phase study including 1) flow; 2) se-

(arrow) (*18*). Stenosis of the upper branch of the left renal artery (D) in a child with renovascular hypertension diagnosed because of [^{131}I]hippurate retention (arrows) after captopril administration, whereas the baseline study was normal. Aortic thrombosis (E,F) in a hypertensive neonate (complication of umbilical artery catheterization): a baseline study with [^{99m}Tc]DTPA (E) showed lack of function of the infarcted left kidney, whereas the right kidney appeared normal (arrow), its function maintained through renin-angiotensin overproduction. When, however, captopril was administered before the repeat study (F), the ischemia of the right kidney became evident as a result of the drug induced decompensation of the renal function; the captopril-induced converting enzyme inhibition caused the ischemic right kidney to cease functioning (open arrow). Acute tubular necrosis (G-I) is manifested typically by a relative preservation of flow (G), a marked reduction of filtration of Tc-GH (H), and a cortical retention of [^{131}I]hippuran (I).

quential imaging with a GFR agent; and 3) renography with HIP, including delayed images with both radiopharmaceuticals. Scintigraphy can usually exclude a congenital or acquired anatomic cause of the RF including obstruction, vascular problems, trauma and focal disorders, and it can indicate the presence of ATN (Fig. 5) (*22*). Prerenal causes of RF are usually recognized clinically, but if such patients are studied with renal scintigraphy they usually show no anatomic abnormality with only a slight decrease in flow, satisfactory accumulation of activity in the cortex and persistent visualization of the collecting system, an image different from ATN. Cortical necrosis conversely will show a lack of flow and function with either GFR or tubular agents.

Initial Evaluation and Follow-up of Obstruction—The Diuretic Renogram

In scintigraphic studies with DTPA, GH or HIP, hydronephrosis and delayed and progressively increasing activity in the collecting system above the level of obstruction are characteristic, but not pathognomonic features of obstructive uropathy. Proper hydration and, particularly, the administration of furosemide help distinguish between obstruction (Fig. 3) and pooling of the urine in a dilated collecting system without anatomic obstruction. The latter includes idiopathic megaureters, extrarenal pelvis, neurogenic bladder (Fig. 4), reflux, and finally, residua of prior obstructive uropathy and reflux, following corrective surgery.

Under these circumstances, it is useful to administer furosemide to induce diuresis which is expected to wash out activity from the collecting system if obstruction is not present. There is not as yet agreement as to which radiopharmaceutical is preferable and at what time after the injection of the radiopharmaceutical furosemide should be injected. We administer 1 mg/kg furosemide intravenously (max 40 mg) 3 min after injection of [^{131}I] hippuran and terminate the examination after 20 min. Others use DTPA or HIP and inject furosemide 15–20 min into the study and prolong scintigraphy for 10–20 min (*22*). In addition, others inject the diuretic 5–10 min before administering the radiopharmaceutical. Performing the diuretic test in the upright position and with catheterized bladder add advantages to the specificity of the procedure.

In general, results of diuretic radionuclide studies correlate well with those of the invasive Whitaker test, in which the pressure in the renal collecting system is measured and compared to the vesical pressure during infusion of saline through a nephrostomy catheter. Hippuran diuretic renography with evaluation of ERPF has particular advantages for initial and follow-up evaluation of obstructive uropathies except when the renal function is substantially impaired.

Diagnosis and Follow-up Of Vesicoueteral Reflux—Scintigraphic Cystography

Scintigraphic (radioisotope) retrograde (direct) cystography or nuclear cystography (Figure 4I), is an accurate and safe procedure with low radiation exposure that can be applied routinely for the diagnosis, semiquantitation, and follow-up of vesicoureteral reflux. The study is performed under continuous scintigraphic imaging in a catheterized patient from the beginning of instillation of the radioactive solution until the patient complains of fullness and discomfort. It is usually concluded by voiding during scintigraphic imaging.

At the University of Miami, we have employed a manometer for quantitative nuclear cystography (*23*): [^{99m}Tc]sulfur colloid (0.5–1 mCi) in normal saline is instilled in the bladder under manometric control. The sensitivity of the test is increased when the filling phase is concluded at 25 cm water bladder pressure rather than when the patient complains of fullness (usually at 15 cm). The voiding phase of the examination is essential since VUR may appear only then, and is of particular significance in patients where pressures >15 cm cannot be achieved. It is not possible to predict the volume of fluid to be instilled to achieve satisfactory pressures (*23*). Monitoring during the entire study is helpful in the diagnosis of reflux, which may be continuous or intermittent and occur at low or high pressure, or only while voiding. The study can also be quantitated (in terms of amount of urine refluxed and pressure and volume of the urinary bladder at the time reflux occurred). A correlation exists between the parameters of the manometric quantitative scintigraphic cystogram and: (a) the renal parenchymal integrity and function (renal scintigraphy with GH) and; (b) the x-ray cystourethrogram (VCU). Initial results indicate that large amounts of reflux (> 3 ml) appearing at low bladder pressures (< 15 cm H_2O) were more commonly associated with renal damage, and that nuclear cystography was more sensitive than VCU in diagnosing, characterizing, and following up VUR (*24*).

CONCLUSIONS AND RECOMMENDATIONS

Scintigraphy is one of the imaging modalities helpful in the diagnostic process and the follow-up of genitourinary problems in infants and children. It provides unique functional/structural information, but has limited resolution and involves ionizing radiation. Thus, it is necessary to specify the clinical indications for scintigraphy as the procedure of choice and as a complementary test; it is equally important to acknowledge the clinical conditions under which scintigraphy may not provide useful or cost-effective information. This knowledge is not as yet complete or documented.

Unfortunately, few practicing pediatric radiologists and adult nuclear medicine specialists are fully aware of the usefulness of renal scintigraphy in pediatric practice. In addition, a limited number of comparative studies between scintigraphy and other imaging modalities has been published. Since scintigraphy is underutilized, indications proposed in the literature of general radiology (*25*) do not necessarily reflect neither the entire spectrum nor the magnitude of the clinical usefulness of this modality.

The following general suggestions for scintigraphy could be proposed, based on published data and personal experience in two pediatric centers and with the current state of the art advances:

1. In the workup of the infant or the child with a urinary tract problem (irrespective of its nature), the single most informative and cost-effective screening test appears to be a three-phase GH study (flow, function phase, delayed imaging). This has yet to be established by extensive comparative studies and requires some qualifications mentioned under the individual indications above.

2. In the asymptomatic infant or child who has never had a urinary tract problem, evaluation of the upper urinary tract should start with ultrasonography, the least invasive and costly procedure. Scintigraphy may be used as a complementary mode; (a) when US is unable to rule out a disorder or (b) when an abnormality is found and functional information is required.

3. There is enough evidence in the literature to support that for functional information (including cortical and split renal function), for follow-up after medical or surgical treatment, and for evaluation of obstruction, renovascular disease, acute infection and vesicoureteral reflux, nuclear medicine studies are indicated as the primary test. US, IVP, or retrograde studies are complementary studies.

4. It is our opinion that congenital and perinatal renal disease can best be evaluated with scintigraphy with GH followed by a x-ray VCU, if distal obstruction is found, to exclude posterior urethral valves. US may help as a complementary test, while IVP rarely has a place.

5. In trauma, CT is the method of choice for reasons mentioned above, but scintigraphy has a high sensitivity as a screening test and it can be used as an alternative or complementary test.

6. In tumor workup, CT or US and, less commonly, IVP are most preferable. Scintigraphy is not the test of choice or even a complementary test, although it can indicate a space-occupying lesion fortuitously or as a screening test. The role of magnetic resonance imaging has to be studied.

Further experience and comparative studies are needed to confirm these views. Knowledge of the indications, techniques, and diagnostic features discussed in this article should increase the utilization of scintigraphy in pediatric nephrologic and urologic patients, amplify our knowledge, and result in improved diagnosis and therapy of these patients.

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