

Sabina Dizdarevic, MD
MSc course in Nuclear Medicine

Supervisor:
Dr.Durval C.Costa, MD, MSc, PhD, FRCR
Senior Lecturer and Consultant

**HOW MAY NUCLEAR MEDICINE TECHNIQUES BE USED TO INVESTIGATE A CHILD
PRESENTING WITH URINARY TRACT INFECTION?
WHAT PRACTICAL PROBLEMS MAY BE EXPERIENCED DURING THE
INVESTIGATION AND HOW MAY THEY BE OVERCOME?**

Institute of Nuclear Medicine
UCLMS, London

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1. INTRODUCTION

In terms of future morbidity and mortality, one of the most important considerations in urinary tract infection (UTI) is the age of patient. In adults, only those with complications or illnesses that fail to respond to treatment require investigation to exclude underlying pathology. In contrast, the young are at a risk of future hypertensive and renal disease; imaging techniques are therefore of paramount importance to identify those with renal parenchymal disease at an early stage and permit appropriate and adequate treatment [1]. Scintigraphic evaluation of urinary tract infection, pyelonephritis, and renal scarring represents a significant portion of a clinical paediatric nuclear medicine practice [2]. However, children are not just a small adults and careful attention to detail and patient care is even more important than with adults [3].

Urinary tract infection (UTI) is a common problem in the paediatric population. Stork proposed a series of definitions in an effort to standardize the diagnosis of UTI. A simple uncomplicated urinary tract infection is defined as an infection confined to the lower urinary tract (bladder, urethra, and ureters). Upper urinary tract infection (pyelonephritis) is infection of renal parenchyma. Asymptomatic bacteriuria is bacterial growth in urine unassociated with clinical symptoms. Significant bacteriuria depends on the method of collection. For a midstream clean-catch specimen, significant bacteriuria requires more than 100,000 colonies/ml, whereas any growth from a suprapubic aspirate is considered significant. The word asymptomatic, however, may be misleading. When questioned after the positive urine culture was obtained, 66% to 76% admitted urinary symptoms, leading Salvage et al to suggest the term covert bacteriuria rather than asymptomatic bacteriuria. The cumulative risk of symptomatic urinary tract infection from birth to 11 years of age has been estimated at 3.0% for girls and 1.1 % for boys.

1.1. CLINICAL PRESENTATION

Unfortunately, the clinical signs and symptoms of urinary tract infection are often nonspecific and misleading. UTI that diminishes renal function is often unrecognized and therefore undertreated. The younger the child is, the signs are more nonspecific. In an outpatient paediatric practice, almost 20% of clinic visits for fever result from a urinary tract infection. If both fever and abdominal pain are considered, that number increases to 31%. Symptoms could include lethargy, irritability, seizure, weight loss, and failure to thrive. Sepsis may occur in as many as one third neonates. Toddlers may present with fever, abdominal pain, vomiting, and diarrhea, as well as feeding problems and failure to thrive. Older children are more likely to have the classic adult symptoms of frequency, dysuria, and urgency with lower tract infection. They are also more likely to experience fever, chills, malaise, and flank pain when pyelonephritis is present.

Although lower urinary tract infection usually resolves without significant sequelae, incorrectly diagnosed or inappropriately treated upper tract infection can lead to renal scarring. Renal scarring can result in hypertension and, with repetitive infection and progressive loss of functioning renal mass, can result in chronic renal failure [2].

2. CLINICAL APPROACH TO INVESTIGATION AND MANAGEMENT OF UTI

Optimal management of UTI in children is important because of risk of permanent renal damage which is greatest in children aged under 2, but diagnosis can be difficult in young children because symptoms such as fever, vomiting, screaming, anorexia, and irritability that may indicate UTI are common in other childhood illnesses such as gastroenteritis and viral infection[4]. Once urinary tract infection has been confirmed by urine culture, a decision must be made about upper tract involvement. But no one test or combination of tests has adequate sensitivity or specificity to be applied to the individual. As a result, clinicians have turned to diagnostic imaging for more reliable information(2).

In 1991, an expert multidisciplinary working group of the Royal College of Physicians proposed guidelines for the investigation and management of children with UTI. The group emphasized the importance of making a bacteriological diagnosis, of instituting treatment without delay after urine sample is taken, and of checking for eradication of infection by means of a follow up urine specimen. The group also recommended that all children, regardless of gender, should have renal tract imaging after a first episode of confirmed urinary tract infection and gave recommendations on the type of imaging for each age group[4]. Before any child undergoes imaging there must be bacteriological evidence of a UTI, i.e. more than 10⁵ organisms of a pure growth in urine [5]. Until the introduction of isotope scintigraphy and ultrasound, the intravenous urography (IVU) was the main investigation of the upper urinary tract [6] and the contrast cystography was the standard screening in order to determine the presence or absence of vesicoureteral reflux in children [7].

It is important to distinguish the group of children with acute pyelonephritis from the one with lower UTI. If renal involvement is present, therapy in these children may be more prolonged in an attempt to prevent long-term renal damage. Nowadays, ultrasonography (USN) should be the initial screening examination of the upper urinary tract in patients with UTI. A child with acute pyelonephritis should have an ultrasound examination on the day of admission and, in absence of hydronephrosis, a 99mTc-DMSA scan within 1-3 days. All patients with abnormal 99mTc-DMSA scans require a follow-up scan 3-6 months later to assess if the defect has progressed to a renal scar. A cystogram is required if an abnormal kidney is found, but this will be 4-6 weeks after the original infection. In girls under 3 years of age DRC (direct isotope cystogram) can be performed, while in those over 3 years IRC (indirect radioisotope cystogram) may be carried out. Boys require MCU (micturating cystourethrogram) to assess the posterior urethra[5] and it is promoted as a means to exclude anatomic abnormalities of the urinary tract, such as posterior urethral valves in boys [7].

Every child with the first proven UTI, but not acute pyelonephritis, requires a full ultrasound examination as well. If this is normal and the girl is over 5 years of age no further imaging is required. A cystogram (MCU) is required in all boys of any age. If the ultrasound is normal and the child is less than 5 years of age, all children require a 99mTc-DMSA scan to exclude scarring. All girl under 1 year of age require DRC to exclude reflux, since the immature kidney is susceptible to damage in the presence of both reflux and infection. If the 99mTc-DMSA scan is abnormal, girls aged between 1 and 3 years require DRC, while those aged 3-5 years require IRC. If the ultrasound and 99mTc DMSA scans are normal in girls aged 1-5 years, then no further imaging is required unless another UTI occurs. If the ultrasound is abnormal, but no hydronephrosis is detected then in girls under 3 years of age a 99mTc-DMSA scan and DRC are required, while in those over 3 years of age a 99mTcMAG3 scan and IRC are required. If hydronephrosis is found then a dynamic 99mTc-MAG3 scan and cystogram are required to exclude an obstruction or reflux[5]. A clear practical

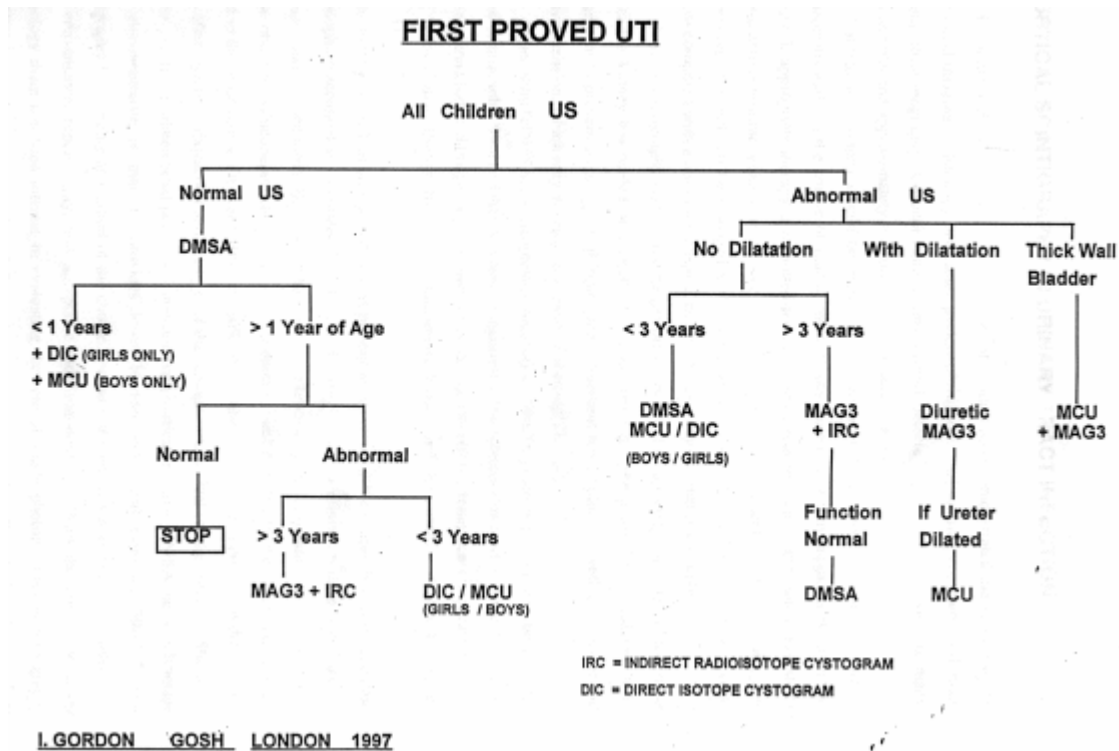
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As above mentioned, nuclear medicine studies (dynamic, and static renography, and indirect cystography as well as GFR estimation) have an important role to play in the localization of infection to the lower or upper urinary tract. Renal cortical scintigraphy (RCS) and radionuclide cystography (RNC) studies can be performed on an outpatient basis in any clinical nuclear medicine department with gamma camera. Sophisticated computer equipment is not needed, and these studies can be achieved within 4 hours during one visit. If stasis or hydronephrosis is present in the kidneys, a diuretic can be given to determine evidence of obstruction. In addition the radiounuclide studies are very sensitive for recognizing congenital malformations such as ectopic location of kidney, or regional functional abnormalities such as duplication and obstruction kidney with significant ureterocele[7].

3. CORTICAL SCINTIGRAPHY IN URINARY TRACT INFECTION

From the mid-1980 to the present, a series of studies have demonstrated the superiority of renal cortical imaging in detecting both acute pyelonephritis and renal scarring compared with both IVU and ultrasonography. Cortical scintigraphy overall detected approximately twice as many defects as USN and approximately four times as many defects as IVU.

Cortical scintigraphy should be performed to document the presence or absence of acute pyelonephritis early in the course of management of any patient in whom diagnosis is suspected clinically. If appropriate therapy is instituted promptly, renal scarring can be prevented. The study may also help determine which patients with clinical symptoms of pyelonephritis do not have upper tract involvement and can be managed with outpatient antibiotics. Cortical scintigraphy is cost-effective compared with a minimum hospitalization of 3 or 4 days to treat pyelonephritis.

Cortical scintigraphy also should be performed as a follow-up study in order to determine whether the kidney has healed or scarred. If scarring develops, the patient will need long-term management to prevent recurring renal injury and subsequent renal failure as well as to detect and treat hypertension, which may develop as a result of scanning [2].

Either ^{99m}TcDMSA(dimercaptosuccinicacid) or ^{99m}Tc glucoheptonate can be used for cortical scintigraphy. ^{99m}Tc-DMSA is now recognized as the reference method to detect focal areas of renal parenchymal damage. This applies to acute pyelonephritis, renal scars regardless of the cause, renovascular disease, the poorly functioning kidney and the complex duplex kidney (see Table 1).

Table 1. Nuclear medicine studies in UTI investigation in pediatrics.

IMAGE STUDY	INDICATIONS
99mTc DMSA SCINTIGRAPHY	Acute pyelonephritis Renal scars regardless of the cause Renovascular disease Differential function The poorly functioning kidney Complex duplex kidney Solitary or ectopic kidney In children undergoing MAGS scintigraphy and IRC for UTI, the high sensitivity suggests that abnormal study precludes the need for a ^{99m} TcDMSA scan.
RADIONUCLIDE SCINTIGRAPHY	Initial diagnosis of VUR in patients with UTI Follow-up of known reflux Postoperative assessment Evaluation of sibling reflux
DYNAMIC RENOGRAPHY(MAG3 SCINTIGRAPHY) /DIURETIC RENOGRAPHY	As a part of IRC Dilatation of any part of the collecting system. ? Obstruction

Approximately 40-50% of an injected dose is present in the cortex 2 hours after injection. The dose of radiopharmaceutical is calculated based on body weight, with a minimum dose necessary for adequate imaging(see later). Because DMSA is a fixed tubular agent, no dynamic excretory images can be obtained. Glucoheptonate is partially concentrated and excreted in the urine and partially bound to the renal tubule. Between 10% and 20% of glucoheptonate dose is present in the cortex 2 hours after injection. Extraction and drainage of the radiopharmaceutical can be obtained. Stasis in a hydronephrotic or dilated renal pelvis will interfere with cortical imaging. DMSA has an advantage over glucoheptonate in that it provides lower bladder and gonad exposure. ^{99m}TcDMSA scintigraphy is emerging as method of the choice , because it combines high specificity sensitivity with convenience, repeatability, and acceptable radiation dose[1]. With the advent of newer technology there has been interest in evaluating the role of single photon emission tomography (SPECT) in renal cortical imaging. It has not yet been shown clinically whether the increased resolution of SPECT renal cortical imaging in children justifies sedation and doubling radiation exposure[2].

Although DMSA has been available and used for over 10 years, there is no general agreement on when to apply the DMSA scan in UTI, i.e. in the acute phase, in the follow-up or both. Factors such as the sort of health care organization, logistics and parental compliance to treatment may influence this decision. Several experimental studies in animals have shown a remarkable agreement between focal DMSA uptake defects and histologically proven pyelonephritis. In many studies the sensitivity and specificity has been over 90%. In recent study of piglets, Codley reported a sensitivity of 80%, but also that minor inflammatory changes could not be seen on scintigraphy. After treatment 70% of the areas with mild to moderate reduction of uptake in the acute phase had normalized at follow up, while areas with initially absent uptake remained in over 90%[8].

The normal DMSA study demonstrates fairly uniform distribution of radiopharmaceutical throughout the cortex. The papillary pyramids and renal collecting systems do not accumulate DMSA and are seen as centrally located photopenic defects covered by a rim of cortex. These defects are particularly well seen on posterior oblique views. There are three recognizable patterns of pyelonephritis:

- a solitary focal defect, involving a portion of one kidney, the defect has mass effect with no evidence of volume loss,
- the multiple focal defects involving either one or both kidney,
- the diffuse involvement of an entire kidney.

Acute pyelonephritis has been shown to be necessary etiologic factor for development of subsequent renal scarring, and the mechanism of renal injury in pyelonephritis has been extensively studied in the experimental models. The rate of resolution of defects due to pyelonephritis is age dependent, occurring more slowly in infants and smaller children and more rapidly in teenagers. With ^{99m}DMSA scintigraphy, the true incidence of scarring with pyelonephritis can now be studied.

Six months is appropriate routine follow-up time. Studies to detect renal scarring should probably not be performed earlier than 3 months after acute infection. However, a study to evaluate a new acute febrile illness can be performed at any time.

Scarring also demonstrates a spectrum of appearances. The hallmark of chronic pyelonephritis or renal scarring is volume loss, either focal or global, in the affected kidney. Volume loss accompanies focal cortical defects or obvious cortical thinning. The scars may be large or small, single or multiple.

The role of cortical scintigraphy in covert bacteriuria, in patients with only lower tract infection clinically, and in siblings of patients with VUR remains to be more fully evaluated.

4. CYSTOGRAPHY IN URINARY TRACT INFECTION

4.1. VESICOURETERIC REFLUX (VUR)

Although a huge amount of literature is devoted to the significance, diagnosis, prognosis and treatment of vesicoureteral reflux, major controversies still exist. When to look for reflux? Which technique is the most appropriate for its detection? How important is reflux as a predictive factor for acute renal lesions or for permanent scarring? Which treatment should be applied? After so many years of experience with cystography, we still need better standardization of methodology[9].

Vesicoureteric reflux is caused by a failure of the ureterovesical valve, which may in turn be caused by a congenital variation, immaturity, or a pathological process. The incidence of VUR in general

population is unknown. A study reports 1% incidence of VUR in group of 536 apparently normal neonates, infants, and children. VUR may be associated with pyelonephritis, which in turn may lead to hypertension and chronic renal failure. Early identification of VUR and assessment of renal integrity are important in children suffering from UTI in order to prevent reflux nephropathy and ultimately, renal damage. However, many studies in recent years have documented that VUR is present in only minority of patients with pyelonephritis. The article by Benador et al emphasizes the changing nature of the diagnosis of UTI in children [7]. There are data that 30% of children with UTI have reflux. 30 % of children with pyelonephritis have reflux as well. 70% of refluxes will resolve spontaneously (grades 1,2,3, but grades 4 and 5 do not resolve). But, probably above 80% children with permanent renal scarring have reflux. The controversy still exists, and further investigations should be performed.

Patients diagnosed with VUR are usually followed by repeated cystographic studies every 6- 12 months to monitor the persistence or resolution of reflux. Prophylactic antibiotic therapy is administered until reflux resolves spontaneously. If reflux does not resolve spontaneously after period of time, which varies for each individual, surgery may be indicated [10].

4.1.2. THE GRADING SYSTEMS FOR VESICoureTERAL REFLUX

If VUR is present it should be graded to the extent possible using the standard international grading system. The Report of the International Study Classification of Reflux (1981) describes five anatomical grades of reflux. These grades are based on the anatomical appearance of the ureters and the renal pelvis and can be visualized by contrast cystography. Because scintigraphy does not have the resolution to visualize calyceal morphology, it relies on the criteria of level reached, dilatation and tortuosity of the ureter, and degree of dilatation of the renal pelvis for the grading reflux. For radionuclide cystography to be accepted by clinical physicians and for it to replace contrast cystography, clinicians must be able to compare scintigraphic results to prior contrast studies. The data from a series of radionuclide cystograms on 844 refluxing ureters are similar (with the exception for the grade I refluxes) to the severity of reflux reported from a series of micturating cystourethrograms, and when grades II and III are combined into low-grade reflux and grades IV and V into high-grade reflux, the correlation was 100% [2]. In addition, Treves et al observe three degrees of reflux in RNC. In the less severe degree (RNC grade I), reflux is limited to the distal portion of ureter without reaching the renal pelvis. This corresponds grade I of the international classification. Distal reflux can be detected only if the reflux is more than about 0.2 ml and is 2 cm away from bladder. More distal reflux cannot be distinguished from scattered radiation from the bladder. A higher degree of severity (RCN grade 2) is characterized by small amount of tracer, reaching the renal collecting system, with either minimal or nonvisualization of the ureter. This corresponds to grade II or II of the international classification. If the radionuclide cystogram reveals a large amount of radiotracer refluxing into a dilated and tortuous ureter accompanied by frank dilatation of the pelvicalyceal system, this is classified as RNC grade 3 and corresponds to the appearance of contrast grade IV and V in the international classification [10]. Also, there is a scintigraphic grading system of reflux into mild, moderate and high grade reflux (see Table 2).

Table 2. Grading system for vesicoureteral reflux

GRADING SYSTEM FOR VESICourethRAL REFLUX PROPOSED BY THE INTERNATIONAL REFLUX STUDY COMITTEE		ATTEMPTS OF SCINTIGRAPHIC GRADING OF VESICourethRAL REFLUX	
GRADE I - Reflux is into, ureter only	GRADE I - reflux is into ureter only	RCN GRADE 1 Grade I radiographically	MILD - Grade I and Grade II radiographically Activity confined to ureter, especially distal ureter.
GRADE II- Reflux fills the ureter, pelvis, and calyces, with no dilation and preservation of the normal sharp calyceal fornices.	GRADE II - Activity in the renal pelvis, but without dilation of pelvis.	RCN GRADE 2 Grade I and Grade II radiographically - A small amount of Tracer reaching the renal collecting system	
GRADE III - adds mild or moderate dilation or tortuosity of the ureter with mild to moderate dilation of the pelvis	GRADE III - Ureters and pelvis are both mildly dilated, but there is no tortuosity of the ureter.		MODERATE- Grade III. Activity extends to pelvicalyceal system.
GRADE IV - Angels of the fornices are obliterated, but papillary impressions are maintained in a majority of the calyces	GRADE IV- Both the ureter and renal pelvis are moderately dilated, with mild to moderate ureteral tortuosity.	RCN GRADE 3 Grade IV and Grade V radiographically - A large amount of tracer refluxing into a dilated and Tortuous ureter and pelvicalyceal dilatation is present.	HIGH GRADE - Grade IV and Grade V Distendent redundant collecting system
GRADE V- Papillaiy impressions are no longer visible in the majority of calyces	GRADE V- The ureter is dilated and has a corkscrew appearance. The renal		

4.2. DETECTION OF VESICourethRAL REFLUX

Three techniques are currently available for diagnosis of vesicorenal reflux: x-ray micturating cystourethrography (MCUG), the radionuclide direct cystography and the radionuclide indirect cystography (Table 3a and 3b).

Table 3a. Indications for cystography

CYSTOGRAPHY		
MCUG	DRC	IRC
Any boy in whom VUR diagnosis should be excluded. Any child with abnormal external genitalia . Any child with thick wall bladder. Any child with abnormal US, with dilatation on US, after	All girls under 3 years of age in whom VUR should be excluded e.g. UTI or prenatal diagnosis of hydroureteronephrosis or with abnormal 99mTc DMSA scan. All boys under 3 years of age in whom VUR has been established on MCUG and in whom follow up	Child who is toilet trained (>3years old) Child with abnormal 99mTc DI scan. Child with abnormal US finding but no dilatation

Table 3b. Comparison between different techniques of cystography (After I Gordon)

	MCUG	DIC	IRC
ANATOMY	+++	-	-
RADIATION BURDEN	+++	-	-
CATHETER	+	+	-
RENAL FUNCTION	-	-	++
BLADDER	-	-	++
PHYSIOLOGICAL	-	-	++
AGE	all	all	>3 years of age
REFLUX	standard	+++	++/-

4.2.1. MCUG

The bladder is filled through an indwelling catheter; images of the filling phase and the voiding phase are obtained. The major disadvantages are the unfavourable dosimetry, fact that only snap shots are available , thus offering possibility of missing some transitory reflux and the invasive character. The advantages of this technique are possibility of grading and demonstration of some morphological changes like urethral valve, ureterocoele, duplicated ureters[9]. Undetected posterior uirethral valves will result in serious renal damage. Any male patient in whom this diagnosis has not already been excluded should have contrast cystography as the initial study. Contrast cystography should be considered in any child with abnormal external genitalia because of increased incidence of structural abnormality of bladder and ureters. In all other patients, including all those in whom ultrasound finds no structural abnormality, the radionuclide cystogram should be the first cystographic study performed.

4.2.2. RADIONUCLIDE CYSTOGRAPHY (RNC)

Although radionuclide cystography was clinically introduced in 1971, it was not until the advent of modern gamma cameras that a modification of the technique incorporating dynamic image became widely accepted[2,7]. Indications for radonuclide cystography are listed in Table 1.

RNC allows a greater than 90% success rate in predicting which patients will have spontaneous resolution of their VUR. The prediction is based on an increase in bladder volume at which VUR occurs on sequential examination. RNC has been recommended as the initial study in the examination of female child with UTI, for the screening of siblings of patients with VUR and in the evaluation of the child with myelomeningocele and is the preferred test for follow up studies[7].

Two forms of radionuclide cystography have been described: direct and indirect. Each method has advantages and disadvantages.

4.2.2.1. DIRECT RADIONUCLIDE CYSTOGRAPHY (DRC)

DRC involves bladder catheterization, draining off the urine and instilling ^{99m}Tc pertechnetate (20MBq) in normal saline until the bladder is full, when spontaneous micturing occur[5]. Conway et al reported systemic absorption ^{99m}Tc pertechnetate across the urinary tract mucosa in 50% of refluxing patients and 20% of patients without reflux. It is theoretically possible to visualize renal excretion and make a false-positive diagnosis of reflux. Similar theoretical concern exist for diethylene triamine pentaacetic acid. Therefore, ^{99m}Tc sulfur colloid is widely used[2,9]. The entire procedure is carried out on the top of a gamma camera linked to a computer system.

The advantages are mainly the high sensitivity of technique in the detection of renal reflux and the possibility of combining this with pressure measurement so that a full urodynamic assessment of the bladder is made. The bladder is visualized during the filling as well as during the voiding and postvoid phase continuously. A urine specimen obtained by catheterization is available for culture. It is now widely accepted that direct radionuclide cystography is at least sensitive and probably more sensitive than contrast cystography. Low radiation burden to the child compared with conventional MCUG, the dose being reduced by factor 20, must also be kept in mind[2,5]. The gonadal absorbed radiation dose is 0.01 to 0.02 mSv, which is 50 to 100 times less than with conventional MCUG[9].

The disadvantages are the need to catheterize the bladder, with the attendant small risk (0.2%) of catheter-induced infection, no anatomical details of the urethra is provided and the presence of catheter and rapid filling of the bladder do not reproduce normal filling and voiding dynamics [5]. The disadvantage is, like for the X-ray technique, the invasive character: no child will accept the procedure without a strong negative reaction[9].

The DRC is indicated in all girls under 3 years of age in whom renal reflux should be excluded, e.g. UTI or prenatal diagnosis of hydronephrosis and in all boys under 3 years of age in whom VUR has been established on MCUG and in whom follow up is required.

4.2.2.2. INDIRECT RADIONUCLIDE CYSTOGRAPHY (IRC)

Indirect radionuclide cystography is obtained as a part of dynamic renal imaging study. IRC should be undertaken in any child who is toilet trained. The child is encouraged to drink before the dynamic study as well as following the study. The child is asked not to void until the bladder is maximally filled. When the bladder is as full as the child can tolerate, a prevoid image is obtained. Usually, after 30-60 min after i.v. injection of radiopharmaceutical (preferable ^{99m}Tc MAG3) the child is asked to void in front of the gamma camera. Boys prefer to stand erect, while the girls sit with their back to the gamma camera. Dynamic images are then recorded continuously during voiding. After voiding is complete, a postvoid image is obtained. Reflux is diagnosed by the presence of more activity in the ureter and renal pelvis during voiding or on the postvoid image than was present just before the initiation of voiding.

The clear advantages of IRC are that it avoids bladder catheterization, allows assessment of both renal reflux and bladder function under physiological conditions, the effect of micturition on upper tract drainage and the difference between a true post-micturition residue and a false residue due to a secondary filling from dilated upper tracts.

There is an increase in radiation exposure compared with the direct technique [2], but radiation burden is still low [5]. There must be enough renal function to concentrate the urine to the point that it can be visualized above background. Enough of the activity in the renal pelvis and ureter must have drained that reflux activity can be distinguished from residual upper tract activity. The indirect method cannot detect those patients who reflux only during the filling phase of the study. Conway and Kruglick reported that 21% of refluxing units were only seen during the filling phase [2], but Willi and Traves showed VUR in only 3% of all kidneys with reflux in their study [5]. Additionally, no urine specimen is available for culture.

Evaluating any technique for the detection of VUR will remain difficult since there is no absolute reference method [5]. It is important to underline that there is tremendous variability of the results from one author to another: some authors, on one extreme find as much as 30-50% false negatives with the direct technique; on the other extreme there is almost no false negative direct cystography, while the rate of false negative indirect cystography can reach as much as 60% [9]. On the other hand, some authors showed that IRC is as sensitive and specific as MCU in detection of VUR [5]. Piepsz et al reviewed 12 studies published in the literature and found 409 refluxing kidneys with both techniques. 294 with direct technique and 274 with indirect technique only. Part of this variability may be due to the fact that reflux is an intermittent phenomenon. However, it is more likely, that the results are depending on the technique which is used and the personal interpretation of the results. More efforts should be put into standardization of both techniques [9].

5. DYNAMIC RENAL SCINTIGRAPHY IN UTI

Dynamic renal scans belong to some of the commonest performed examinations in paediatrics and are indicated:

- Whenever there is dilatation of the collecting system, then both differential renal function and drainage can be assessed.
- Whenever surgery on the renal pelvis or ureter is planned.
- When indirect radionuclide cystography is required.
- Follow up after renal transplantation when blood flow must be assessed.
- If differential function is required for any other reason.
- A diuretic is required whenever there is dilatation of any part of the collecting system.
- When investigating a child with sustained systemic hypertension [12].

The only time a dynamic renogram may provide inadequate differential function is in the presence of very poor renal function and when there is an ectopic kidney present. In these circumstances DMSA is isotope of choice [12]. In patient with unilateral hydronephrosis dynamic renal scintigraphy in 25% has shown 'supranormal' renal function. The explanation for this finding is unclear, but in most cases it is caused by technical problem, likely the inadequate background subtraction of mercaptoacetyl triglycine in the liver [13].

Dynamic renal scintigraphy plays a role in investigation of child with UTI when IRC is required and diuretic renography is useful tool for the investigation of the various causes of hydronephrosis of that of obstruction [4,15]. Hydronephrosis (HN) and hydroureteronephrosis (HUN) is a common finding

in the workup of patients with UTI. There are multiple causes for HN and HUN, including vesicoureteral reflux, UTI, previous obstruction (urethral valves), congenital malformations (prune-belly, megacalyces/ megaureter), noncompliant bladder, and urinary tract obstruction (congenital stenosis, tumour, lithiasis). The commonest hydronephrosis seen is that of the dilated renal pelvis, usually referred to as uretero pelvic junction, in which the question of obstruction is raised, since a dilated PUJ does not require surgery [15]. The definition of obstruction is generally taken as a failure of drainage following a diuretic stimulus, yet more attention is now paid to the combination of the function of the kidney as assessed in the first 1-3 min, the degree of dilatation and washout following diuresis. In paediatrics dynamic renal scans are generally carried out in the supine position, and thus failure of drainage may be related to the absence of the effect of the gravity. However, the other causes for poor drainage include a full bladder, massive dilatation and very poor renal function [5]. Another important factor affecting the outcome of diuretic renography is the patient's state of hydration. The diuresis response is dependent on the availability of fluid within the tissues to produce urine and respond to the diuretic stimulus [14].

The differential function is calculated using the Patlak-Rulland plot which is a simple robust technique, avoiding the detrimental effect of blood background.

Some investigators advocate the use of mean transit times as a further quantitative parameter useful in the diagnosis of obstruction. However, its use in paediatrics is limited due to the poor statistical information gained from the small cortex in children which renders deconvolution unfeasible [14].

Of the ^{99m}Tc labelled compounds either DTPA or MAG3 can be used. If one wishes to achieve high reliability and reproducibility in the analysis of the renogram, especially in the infants then there are good reasons to choose MAG3:

- The biodistribution of MAG3 is mainly intravascular. MAG3 is bound to plasma protein. This is very important especially in children under 2 years of age because of the relatively large extracellular space. Using DTPA, which is freely diffusible from the intra to extravascular space (DTPA is a small molecule, not bound to plasma protein crosses the capillary membrane easily), the amount in the intravascular space is small and so the kidney is presented with small concentration of isotope compared to MAG3.
- The rate of maturation of the glomeruli and tubules is different. The GFR rises steadily over the first two years from approximately 30ml/min/1.73m² at birth to 80% of the adult value by that stage. The tubules, on the other hand, mature more rapidly and have reached 90% of the adult value in the handling of MAG3 by 6 months of age. MAG3 is excreted by the proximal tubules of the kidney, while DTPA is excreted via glomerular filtration. This results in the extraction fraction of MAGS from the kidney being much greater than DTPA [5,12].
- If indirect radionuclide cystography is undertaken, the higher renal extraction and subsequent low background make MAGS the tracer of choice. It is rapidly cleared from the blood stream by tubular secretion and is not retained in the parenchyma of normal kidneys, leading to high target-to-back-ground ratio and excellent imaging characteristics [13,15].
- If diuretic renography is undertaken MAG3 has several advantages that include a rapid renal clearance and primary excretion by tubules on which furosemide acts. In the presence of obstruction or poor renal function, the absorbed radiation dose to the patient will be less compared with other renal radiopharmaceuticals [15].

Patients undergoing diuresis renography should be at least 1 month old to reduce the likelihood of immature renal function significantly affecting results. As above mentioned newborns have a lower glomerular filtration rate (GFR) than older children. The 'immaturity' of the kidney may alter the renogram pattern, and could affect diuretic response. Premature infants should be older than 1 month

before the initial study, since their tubular function is even less likely to adequately respond to a diuretic stimulus [15].

A diuretic renogram in any child, including an infant, may be undertaken with child supine on the gamma camera face with diuretic (furosemide 1mg/kg) usually given at 18-20 minutes after the isotope. Post-micturition views at 40 min are possible if the child is allowed to go to the toilet after 30-40 min. Infants and toddlers may simply be held on parent's shoulders for 7-8 min, during which time micturition will occur in the vast majority of cases [5].

6. PRACTICAL PROBLEMS IN PAEDIATRIC NUCLEAR MEDICINE

Performing effective nuclear medicine procedures in the paediatric population requires certain modifications of techniques used when studying adult patients [16]. A visit to the nuclear medicine department can be a upsetting experience for both the child and parents and several modifications and factors must be taken into account to obtain good quality scan and to minimize their anxiety.

6.1. PREPARATION

Good practice includes full preparation of the child and parent for investigation [5]. Providing information concerning the procedure is one of the first conditions to obtain the cooperation of the patient and to relieve his/her anxiety. The referring physician gives the parents the first information. However, parents are emotionally involved and therefore often unable to absorb this information and to organize their thoughts at that moment. It is recommended to give an information leaflet about procedure. They are then more capable to prepare the child for the planned procedure. However, additional explanation to the child is needed once it arrives in the department [17]. The attitude of every member of the department must be positive, reassuring and sympathetic: this includes the reception staff as well as professionals. They should be adapted to the age of children, be direct and honest, and include what the child may feel, see and hear [17]. Patience, common sense, imagination and flexibility are desirable personal qualities which will assure a favourable atmosphere. It is important that everybody involved really enjoys working with children and feels at ease with them. Children should feel that every effort has been made to make premises comfortable as well [18]. The stress of the surroundings can be decreased by making the typical hospital environment of the department more comforting, cheerful and familiar.

6.2. DOSE SCHEDULE

The dose of isotope must be scaled down according to either body surface area or body weight. The use of age as a scaling factor is not recommended since the children in chronic renal failure may fail to grow normally [5]. The radiopharmaceutical dose schedule suggested comes from the paediatric task group of European Association of Nuclear Medicine (EANM) (see Table 4a and 4b) [5].

Table 4a. Radiopharmaceutical dose schedule in paediatric nephrourology

RADIOPHARMACEUTICAL	ADULTS (MBq)	MINIMUM PAEDIATRIC DOSE
99Mtc-DTPA(kidney)	200	20
99mTc-MAG3	100	15
99mTc-DMSA	80	15
99mTc-Pertechnetate (DIC)	20	20

Table 4.b Dosage recommendation of the Peridatric Task Group of the EANM as a fraction of adult administered activity.

3 kg =0.10	22 kg =0.50	42 kg = 0.78
4 kg =0.14.	24 kg =0.53	44 kg = 0.80
6 kg =0.19	26 kg =0.56	46 kg = 0.82
8 kg =0.23	28 kg =0.58	48 kg = 0.85
10 kg =0.27	30 kg =0.62	50 kg = 0.88
12 kg =0.32	32 kg =0.65	52-54 kg =0.90
14 kg =0.36	34 kg =0.68	56-58 kg =0.92
16 kg =0.40	36 kg =0.71	60-62 kg =0.96
18 kg =0.44	38 kg =0.73	64-66 kg =0.98
20 kg =0.46	40 kg =0.76	68 kg = 0.99

6.3. INJECTION

Fear of venepuncture is a reality for most children, and is quite often a major source of worry for the child, the parents and sometimes also personnel. In order to perform venepunctures successfully, consideration must be given to practical matters such the use of local anaesthetic and possibly most important of all, aspects of care[18]. Eutectic mixture of local anaesthetic cream (EMLA) should be applied 45 min before examination. This allows ample time for adequate fluid intake if a dynamic scan is to be undertaken (at least 100 ml even for the infant). Venepuncture must be performed by skilled personnel. The injection should be done using a butterfly needle with three-way tap so that minimal manipulation of the needle is required[5,14].

6.4. IMOBILIZATION / SEDATION

Effective immobilization is extremely important to ensure good quality images. The various methods for gaining patient cooperation and immobilization may be tried. In the youngest age group, neonates to 2 years, simply holding the patient in place may be sufficient. Other techniques, such as sleep deprivation before the imaging procedure and feeding the child a bottle on the imaging table, may be equally successful in some patients. The use of sand bags, Velcro straps or if available vacuum extractor mattress and entertainment such as television, music, or reading stories also may be successful in patients older than 4 or 5 years age. Frequently, child may be so frightened, especially

of the injection, that cooperation is impossible until his/her fears are allayed[19,5]. Parents are encouraged to stay with their child throughout the imaging procedure to support and amuse it with toys or books they have brought or that are available at the nuclear medicine department. Tired or agitated children might be better off with lights turned down and the opportunity to sleep[12]. It is important to listen carefully to the specific needs of the child. If possible, young children are examined during their day-time sleeping period. The favourite cartoon or film can be watched during the imaging. Sedation is not routinely required. There are, however, "difficult' children especially between ages 18 months and 3 years, in whom sedation helps. The most common indications for sedation are:

- pronounced fear of venepuncture
- inability to cooperate during imaging
- mental disability to cooperate,
- past bed experiences; hospital fear[20].

In such cases oral chloral hydrate is useful. Intranasal sedation with Medazolan is gaining popularity since its action begins within 2-3 min but lasts only 20-30 min [5].

7. CONCLUSION

Nuclear medicine .studies of renal investigation have gained popularity because of their relative speed, simplicity and ability to estimate split renal function. These factors are particularly important in the paediatric population in whom studies which are noninvasive and associated with minimal risk and discomfort are advantageous such in the assessment of urinary tract infection. Radionuclide studies of the kidney provide a simple noninvasive method of estimating total and individual renal function [13]. ^{99m}Tc DMSA is useful in evaluation split renal function, to distinguish between acute pyelonephritis and cystitis, and to assess changes in function and development of scarring over the time. while radionuclide cistography has proven to be a sensitive indicator of reflux[21]. Diuretic renography is commonly performed in children with hydronephrosis, providing noninvasive quantitative information on the degree of obstruction and renal function.

Adequate preparation, pleasant surroundings adapted to children, relaxed atmosphere where parents and children are made to feel welcome by experienced and dedicated personnel are the most important conditions for obtaining scans of high technical quality[22].

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