**Child-Adult Interface**

**Cortical scintigraphy and urinary tract infection in children**

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**Introduction**

Detection of renal cortical lesions by means of radioisotopes is one of the most widely used techniques in the field of paediatric nuclear medicine. Various substances have been proposed for that purpose, but there is presently a wide consensus on the preferential use of dimercaptosuccinic acid (DMSA) labelled with Technetium-99m. This tracer was introduced in 1974, but it is only since the late 1980s that numerous publications have appeared, related to the methodology, the robustness of the technique and the field of clinical applications.

**Methodological aspects of Tc-99m DMSA scintigraphy**

About 4–8% of the injected activity is excreted after 1 h and 26–30% after 14 h, while 40–50% of the activity accumulates in the kidney after 6–7 h. The tracer is taken up by the proximal tubular cells, directly from the peritubular vessels, and is therefore located in the outer layer of the kidney with minimal activity in the medulla and the calyces. As a consequence, the posterior view of the DMSA scintigraphy will usually not appear homogeneous, the inner part of the kidney showing less uptake than the outer part. In two main conditions, however, the excretion of the tracer can significantly interfere with the interpretation of the images. In pronounced hydronephrosis with marked delayed transit, the excreted renal activity may accumulate into the calyces and pyelum, altering artificially the intrarenal tracer distribution. In Fanconi syndrome, the DMSA escapes the tubular cell and is found mainly in the urine, resulting in low renal activity.

Alternative tracers for renal imaging are those with high excretion rate used for renography, such as Tc-99m MAG3 and I-123 Hippuran. They offer the advantage of combining cortical imaging with information about renal excretion. They are, however, less accurate for the detection of cortical defects.

Radiation dose to the patient is low. The effective Tc-99m DMSA dose is estimated to approximately 1 mSv examination regardless of the age of the child and using the dose schedule put forward by the European Paediatric Task Group. This is generally less than the mean intravenous urography doses.

**Sensitivity and specificity**

Studies on the sensitivity of the technique are generally based on comparison with intravenous urography or ultrasound. In children with urinary tract infection, there is much evidence that DMSA scintigraphy is more sensitive than the two other techniques in acute lesions as well as in the detection of late sequelae. In contrast, scintigraphic abnormalities are not specific: in case of acute urinary tract infection, regional defects can be due to acute infection but also to any other underlying disease such as renal abscess, hydronephrosis, cysts or duplex kidney with abnormal upper or lower moiety. It is therefore mandatory to combine scintigraphy with a technique allowing differentiation between these situations: ultrasound has a low sensitivity for acute pyelonephritis but is useful to exclude any expansive lesion or huge dilatation of calyces and pyelum. In the absence of clear ultrasound abnormality, the diagnosis of pyelonephritis on the basis of DMSA lesions becomes much more obvious.

How well is the technique of DMSA scintigraphy validated? Animal models combining vesicorenal reflux and infection [3–5] have shown the relation between the extension of the anatomical lesion and the presence of a scintigraphic abnormality. DMSA scintigraphy...
is normal in the absence of anatomical lesions and only small lesions are missed by DMSA scintigraphy.

Interpretation of images obtained

How good is interobserver reproducibility in reporting on DMSA scintigraphy? Poor concordance as well as good concordance has been observed. A recent large study involving a great number of nuclear medicine physicians revealed a high concordance on normality or abnormality [6]. Standardization of the conditions of the procedure is, however, mandatory and much effort has been devoted recently to the production of consensus and guidelines in this field [7,8]. A point of main importance is that having an immobile child during the whole acquisition is mandatory for the quality of the image. Drug sedation can, however, generally be avoided. An empathic attitude toward the child, a well-trained technologist for paediatric procedures and involved parents before and during the procedure are generally effective.

The interpretation of the images is generally easy, although one should be aware of the existence of several normal variants, including spleen impression, variability in the shape of the renal contours, number and size of the columns of Bertin, persisting foetal lobulation, poles appearing as hypoactive. Lesions are described as single or multiple, small or large, with or without volume loss; the renal contours can be normal, indistinct, irregular or absent; the kidney can be small or swollen. When observed during the acute phase of pyelonephritis, hypoactive areas without deformity of the contours are likely to become normal at a late control, while deformed contours often correspond to renal sequelae. It is, however, not recommended to conclude on the presence of renal sequelae on an ‘acute’ DMSA. Permanent lesions can only be reported on the basis of late control studies, at least 6 months after the acute infection [7].

Determination of left and right relative DMSA uptake is an accurate and robust quantitative measurement, except for patients in renal failure in whom the signal to noise ratio is particularly unfavourable. Therefore, this simple measurement should be systematically added to the scintigraphic images. It has been shown that interobserver reproducibility of relative function measurement is generally good. The normal lowest value for relative uptake is somewhere around 45%. To be noted that normal relative uptake can miss completely the case of bilateral small kidneys; inversely, the normal unilateral duplex situation can be associated with abnormally high relative function.

Place in management of urinary tract infection

The field of highest controversy is probably the place of cortical scintigraphy in the strategy of investigations in urinary tract infection.

The technique is nowadays considered as the best one for the demonstration of unilateral or bilateral renal sequelae, replacing progressively intravenous urography [7]. The role of ultrasound for that purpose is limited owing to its poor interobserver reproducibility. Several questions are still unresolved. In a population of children with acute pyelonephritis, what is the frequency of late renal sequelae? The answer is essentially variable from author to author and is dependent on the type of patients included in the study, the retrospective or prospective character of patients’ inclusion, the delay between acute infection and late DMSA. Moreover, the health care system and treatment regimens have changed during the last decades and the number of renal sequelae might have decreased. Recent prospective work has shown that no more than 10–12% of patients with clinical acute pyelonephritis will remain with renal sequelae on the 6-month DMSA scintigraphy [9]. Is the frequency of sequelae higher when acute pyelonephritis is associated with reflux? The literature related to that point is even more confusing, the timing of late DMSA scintigraphy and the grade of reflux being often not taken into account. Large surveys [10] tend to confirm, however, that the association of acute pyelonephritis and dilated reflux will give rise to a far more important number of DMSA renal sequelae. What risks do DMSA sequelae represent, as far as pregnancy complications, hypertension or renal failure are concerned? The answers will come only from long-term follow-up of patients with this kind of lesion. How often, in the absence of relapse of infection, will the 6-months DMSA become abnormal if the ‘acute’ DMSA was normal? Although some authors describe this kind of unfavourable evolution, it is generally accepted that late DMSA will remain normal [7].

Several authors are sharing the idea that ‘acute’ renal scintigraphy is not necessary, because many of the acute lesions are transitory and will disappear at a late control. Moreover, the diagnosis of complicated UTI is generally based on clinical and biological data and scintigraphy is often considered as not necessary for the purpose of diagnosis. Finally, there is at the present time no single strategy based on the acute scintigraphy, as far as further investigations or treatment are concerned. Those in favour of ‘acute’ DMSA consider that clinical and biological arguments constitute only weak evidence for acute pyelonephritis: patients with lack of clinical and/or biological signs or with negative or equivocal urine cultures may still have urinary tract infection with obvious acute renal lesions; patients with full clinical picture of complicated UTI may or may not present with abnormalities on renal scintigraphy.

Another point is that the best predictor of renal sequelae is probably the presence of a DMSA abnormality during the acute phase of infection. The early definition of such a high-risk group may be of interest, particularly in geographical areas where the compliance to treatment and follow up is low.
Well-controlled prospective studies are needed in order to estimate whether or not an early scintigraphy may influence the type and the duration of the treatment in case of high probability of acute pyelonephritis, or modify the further strategy (such as the indication for a micturating cystourethrogram or for a late control of renal scintigraphy).

Economic issues related to this topic are still debated, some considering the price of acute DMSA as unacceptable, some others underlining the much higher price of prolonged intravenous treatment.

References