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Review article

Paediatric nuclear medicine

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Abstract. Until the 1980s no serious attempts were made to develop paediatric nuclear medicine, as for various reasons many centres were reluctant to perform radionuclide examinations on children. Then two books were published on paediatric nuclear medicine in 1984 and 1985, respectively. In 1987, a group of physicians formed an informal club of paediatricians and nuclear medicine specialists in an effort to improve the relationship and cooperation between these specialties. Carrying out nuclear medicine examinations on children requires a completely different approach than on adults. Suggestions are made and tips given, and the specific problems involved are discussed in detail.

Key words: Paediatric nuclear medicine – State of the art – Understanding the special problems

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Paediatric nuclear medicine in Europe

In 1983, a questionnaire was sent to 600 European centres of nuclear medicine requesting information on the number of paediatric examinations carried out. There were 279 replies from 20 countries. The total number of children examined in these centres was just over 64,000 for the year 1983. This number is rather limited if we compare it with the mean yearly activity of a department of nuclear medicine. As a matter of fact, paediatrics is the Cinderella of nuclear medicine and many centres remain reluctant to perform radionuclide tests in children for reasons explained later in this article.

Nuclear medicine is recognized as a safe and non-invasive procedure in children in North America; since 1974, several books exclusively devoted to this subject have been published (James et al. 1974; Handmaker and Lowenstein 1975; Alderson et al. 1978; Sty et al. 1983; Siddiqui 1985; Treves 1985). Moreover, since the early seventies, several paediatric activities have officially been developed by the American Society of Nuclear Medicine: scientific sessions devoted exclusively to paediatric topics have been organized at the annual meeting of the Society, as well as teaching courses covering the main fields of paediatric nuclear medicine. An informal and open "paediatric club" was created and, for many years, has come together during the annual meeting, allowing better contact between the physicians involved in this particular aspect of nuclear medicine, stimulating all kinds of collaboration, as well as extensive exchange of information.

In Europe, except for some valuable individual efforts, it is noteworthy that during the seventies no serious effort was made to develop paediatric nuclear medicine. This is rather surprising since fundamental work on functional radionuclide examinations, particularly the kidney (which in Europe is the main field of work in paediatric nuclear medicine), has been accomplished in European laboratories: basic work on renography (Britton and Brown 1969, 1971); the methodology of quantification of renal function with mercury bichloride (Raynaud et al. 1968), overall chromium 51 ethylene diaminetetra-acetic acid (EDTA) clearance measurements (Chantler et al. 1969; Brochner-Mortensen 1978), separate clearance calculation by means of external detectors (Oberhausen and Romahn 1968; Piepsz et al. 1977); study of the transit times (Diffey et al. 1976; Kenny et al. 1975; Erbsmann et al. 1977), diuretic renography (O'Reilly et al. 1979); and indirect cystography (Eissner et al. 1975; Hahn et al. 1975).

During the 1980s, things changed. Two books on paediatric nuclear medicine were published: one in 1984 (Hahn and Reither) on nuclear medicine and ultrasound

and one in 1985 (Gordon), integrating paediatric nuclear medicine in the strategy of medical imaging. In 1984, a paediatric task force was created, covering both existing European societies of nuclear medicine, the ENMS and the SNME. In 1987, with the establishment of the EANM, an official Paediatric Task Group has been approved. The first purpose of this group is to elaborate on and bring to realization multicentric projects, e.g. a retrospective work on foreign-body inhalation was readily achieved and published (Piepsz 1988). A schedule of the radioactive doses commonly used in children by different European physicians has recently been published (Gordon 1990).

The second purpose of the task group is to stimulate new paediatric interests in Europe: for several years, an informal and open paediatric meeting has taken place at the annual meeting of the EANM. Despite the rather limited experience of this group, an atmosphere of friendship and cooperation has already developed. It is hoped that the group will help in improving contact between the paediatrician and nuclear medicine specialist. In reality, the nuclear medicine specialist ignores some of the specific needs of the paediatrician and, similarly, the paediatrician is not aware of the possibilities offered by nuclear medicine procedures. The task group published a paper called "The role of nuclear medicine in paediatrics" in a paediatric journal to educate paediatricians about the usefulness of radioisotope techniques (Ciofetta et al. 1988). It is mandatory that paediatric papers on nuclear medicine topics should more frequently be published in European paediatric journals.

General approach for paediatrics

The vast majority of the 64,000 nuclear medicine examinations carried out on children during 1983 were in general departments of nuclear medicine where no special paediatric facilities were available. Children are not small adults, and the professional staff must not forget that children understand far more than one gives them credit for. This means that it is mandatory that *all* of the staff speak directly to the child. The parents can, of course, join in the discussion. This approach makes the child feel that he/she is the focus of the visit and allows the child to behave in the most advantageous way. The object is to end up with a high-quality study and a child plus parent who feels well treated. This does not mean that the child cannot cry or express his/her concern or anxiety but that one would like the child to cooperate during both crucial periods when the injection is being given and the actual image acquired.

In a general nuclear medicine department, one should not attempt to fit in a paediatric examination between two adult patients since the nuclear medicine examination in the child always takes longer than in an adult. A list of adult patients scheduled for the day with a child in the middle of such a schedule causes the technician to feel rushed, a feeling readily conveyed to the child, resulting in an uncooperative child and an irate technician. The child is sensitive to pressure and the child's cooperation disappears rapidly when he/she feels this sort of pressure. It is far better to dedicate one morning or afternoon a week entirely to paediatrics. Each paediatric examination should be allotted twice as much time as for an equivalent adult examination. This would also allow the creation of a small waiting area where a low table, paper and a few coloured pencils, as well a selection of appropriate books, would result in the child being occupied prior to the examination. This allays the anxiety about the impending examination.

The word "paediatrics" can be used to identify the majority of factors as to why children's examinations are special.

P = Prepare the child and the parents with an adequate appointment letter; on the day of the examination, allow them to see the equipment before anything is done to the child.

A = Assess the child and parent as to the cooperation you can except so that the potential need for sedation is established.

E = Explain fully to the child and parent what is going to happen, step by step. In this way, the child develops confidence in the team.

D = Dose: this should be scaled on a body surface area/weight basis (explained later).

I = Injection: a butterfly needle connected to a three-way tap is normal practice, so that the isotope syringe can be adequately flushed without disturbing the needle. Using this technique allows access to small veins, which would be difficult with an ordinary needle. If no one in the nuclear medicine department has any experience with injections in children, then arrangements with the resident paediatric junior medical staff should be made. This is easier if all paediatric examinations are grouped together on certain days of the week.

A = Amuse the child both before the examination and during the actual study. Appropriate books, a radio/cassette with stories and/or music are useful. Encourage the parent to amuse the child.

T = Technique: the technician should adapt his/her technique to the needs of the child. The most important images should be obtained first, e.g. when carrying out a bone scan, the anterior and posterior views of the pelvis should be done as soon as the child has micturated – usually the first images.

R = Reduce the images to the minimum as far as time is concerned, but make sure that adequate information is obtained, e.g. a pin-hole view of the hip in an uncooperative child may be reduced to 3–5 min if there are high-quality images of the pelvis.

I = Immobilize the child. This is easily carried out using either sand bags on either side of the child with velcro straps or the use of the mattress from which air

can be let out. Encouraging close contact between child and parent throughout the examination reduces the child's attempts to move in many cases.

C = Camera: the camera should be placed with the collimator upwards, so that the child can lie on top of the camera. In this way the child is rotated and the camera is kept constant. This provides the child with nothing above him/her. There are exceptions to this rule, e.g. abdominal scans for ectopic gastric mucosa, renal transplant and cardiac studies.

S = Sedation: when all the above procedures have been taken into account, then only about 5% of children require sedation. These children are usually between 18 months and 4 years of age. The particular sedative used should be the one with which the paediatrician/nuclear medicine physician is most familiar. Certain institutions have reported that at times sedation changes a difficult child into an impossible child.

Radiation

In many developed countries, the typical levels of absorbed dose delivered over a short period in diagnostic radiology and nuclear medicine per examination are about 1 mSv on average to each individual and until recently have been considered to be similar to the dose associated with 1 year's exposure to natural background (ICRP publication 52, 1987). This natural background is probably underestimated and radon may be responsible for 55% of the sources of ionizing radiation, leaving only 4% for nuclear medicine (Tilyou 1990). That means that the radiation risk related to a nuclear medicine examination is low and tables have been published comparing this risk level to similar low daily risks (Roedler 1984).

However, one should be aware of the high number of examinations using ionizing radiation, despite the increasing use of imaging techniques like ultrasound or magnetic resonance. Medical radiation exposures are mainly related to diagnostic radiology (300–900 examinations per 1000 inhabitants in developed countries), but nuclear medicine procedures are also of significance (10–40 per 1000 inhabitants) (UNSCEAR 1982).

The longer life expectancy of children allows further expression of the radiation exposure risk than in the adult. It is obvious that the reluctance of both the nuclear medicine physician and the paediatrician to deal with radionuclide investigations is still related mainly to the dosimetric problems.

In a recent report (ICRP Publication 52, 1987), the International Commission on Radiological Protection have made some recommendations, part of them being specific for children:

– An in vivo nuclear medicine procedure should first take account of the availability, relative efficacy and associated risk of alternative methods like ultrasound, magnetic resonance imaging or in vitro tests.
– The paediatric patient is subject to all the basic considerations of radiation protection in nuclear medicine but, in addition, special consideration should be given the physical and biological factors that are unique to the child. The biological distribution, uptake and retention of radiopharmaceuticals vary considerably throughout childhood and need to be taken into account (Eißner and Wolf 1980). An example is the absorbed dose to the epiphyseal regions of growing bone, particularly for gallium 67 (Gelfand 1983), and dosimetric considerations may modify the risk-benefit ratio in a child.
– The activity administered to children should not exceed that required to provide the necessary clinical information; it should be derived from a scaling factor adapted to the adult dose, yielding an approximately equal count-rate density. Various tables have been published, one of them being recommended by the European Paediatric Task Group (Gordon 1990). It is obvious that nuclear medicine procedures should not be used for screening purposes in children or for determination of "normal values". On the other hand, it can be accepted that for technetium 99m and iodine 123, the dosimetric considerations are not significant if the clinical indication of the examination is correct (Roedler 1984).
– Any tendency to limit the administered amount of activity below the optimum, even for well-intentioned reasons, will usually lead to poor-quality images and diagnostic errors. Minimal doses for the usual nuclear medicine examinations are available in the literature (Gordon 1990).
– Due to the short effective half-life of most diagnostic radiopharmaceuticals, there is usually very little radiation hazard to the patient's family. Nevertheless, even the very small doses that might be received can be avoided by minimizing prolonged intimate contact between a patient and members of the family during the first few hours after administration of a diagnostic radiopharmaceutical.
– Irradiation of the fetus results from placental transfer and distribution of radiopharmaceuticals in the fetal tissues (pertechnetate in the fetal thyroid during the last two trimesters of pregnancy). External irradiation from a radiopharmaceutical present in the mother (tracers rapidly eliminated by the kidneys, for instance) is also a source of radiation exposure to the fetus. The risk of irradiating the fetus should be compared to the risk of either not making the diagnosis or using other techniques to make the diagnosis. The increased risk from fetal irradiation as a result of a diagnostic procedure is low, however (Taylor 1979; Hahn et al. 1980).
– Finally, many radiopharmaceuticals are secreted in breast milk, and recommendations have been published in order to minimize the exposure of the breast-fed child (Ahlgren et al. 1985; Coakley and Mountford 1985). For instance, nursing should be stopped for at least 12 h for most of the ^{99m}Tc compounds.

Specific problems related to nuclear medicine procedures applied to children

Uronephrology

^{99m}Tc-dimercapto succinic acid (DMSA) is considered to be a sensitive agent for the detection of regional cortical impairment in children, particularly in acute pyelonephritis (Handmaker and Lowenstein 1975; Gordon 1987; Verber et al. 1988; and Meller 1989; Tappin et al. 1989; Verboven et al. 1990) and in reflux nephropathy (Merrick 1980; Tamminen et al. 1978). The images are usually performed 2 h after intravenous injection of the tracer; they should be delayed up to 4 h if the bladder activity is high, suggesting significant urinary activity that could interfere with interpretation of the renal images. The normal renal image is heterogeneous. In posterior projection the periphery shows high activity, contrasting with the hypoactive areas in the central part of the kidney due to the presence of the renal pyramids. Strips of hyperactivity, in variable number and location converging from the periphery of the kidney to the hilus, are normally seen and correspond to the columns of Bertin. A good-quality image requires visualization of those contrasts (Fig. 1). However, they are often not observed in the child under 3 months of age. Moreover, in these young infants, the renal uptake of DMSA is low, and high background activity (liver, bone marrow and extravascular space) may obscure the image (see section on neonates).

Pin-hole views are helpful in infants; left and right oblique views are required in all age groups. Acute pyelonephritis usually presents as a large hypoactive area, generally located at the upper or the lower pole of the kidney without deformation of the outlines of the kidney (Fig. 1). Although not specific, this image is highly suggestive of acute pyelonephritis, especially in the absence of structural changes on ultrasound, e.g. like localized hydronephrosis, abscess, or cysts. Other patterns may be observed like multiple disseminated hypoactive areas or simply diffuse hypoactivity of the whole kidney. All these changes may disappear slowly under adequate treatment, but it is not unusual for them to remain unchanged several months after treatment. It must still be demonstrated whether these permanent changes will later on give rise to typical sequelae of chronic pyelonephritis, such as those described on intravenous urogram. In chronic reflux nephropathy, the DMSA changes are different: the most striking feature is a kidney of small dimensions, with major deformities of the outlines and peripheral defects (Fig. 2). Sometimes the lesions are less pronounced and consist only in deformation of the normal renal contours, the kidney size being normal. The normal contours are generally convex, except at the external upper part of the left kidney, corresponding to the impression of the spleen. Concave or flat contours may suggest the presence of renal lesions.

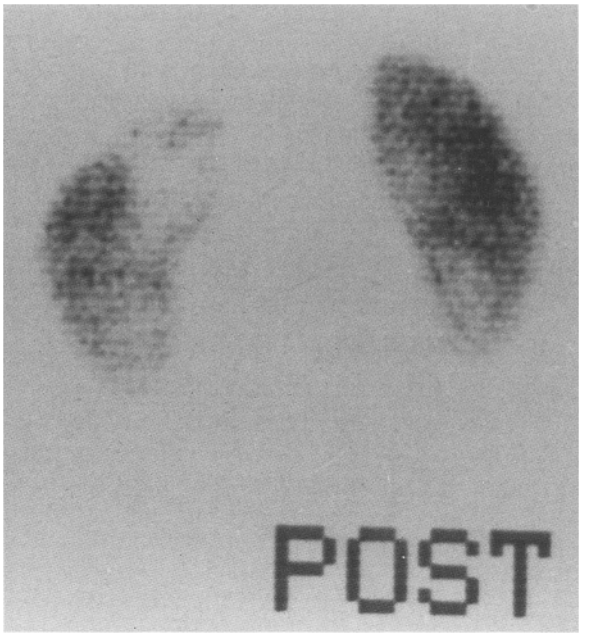

Fig. 1. ^{99m}Tc-DMSA scintigraphy (post view) in a 5-year-old child. First urinary tract infection. The normal renal cavities are well delineated as hypolucent areas, separated by strips of hyperactivity, converging from the periphery of the kidney to the hilus. A large hypoactive area is seen at the upper pole of the left kidney, without deformation of the renal outlines, thus suggesting, in the absence of structural abnormalities on ultrasound, the diagnosis of left acute pyelonephritis

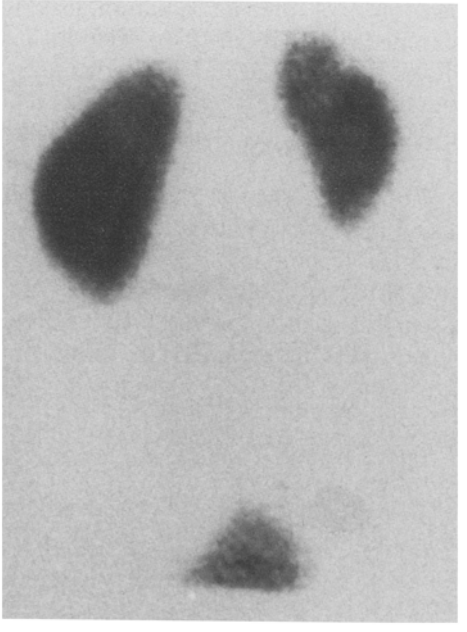

Fig. 2. ^{99m}Tc-DMSA scintigraphy (post view) in a 2-year-old child. First urinary tract infection. The right kidney is small; its outlines are irregular with a sharp defect at the external part of the upper pole, suggesting chronic lesions probably associated with vesicoureteral reflux. The left kidney seems normal: the external part corresponding to the cortical area, is hyperactive, while the inner part corresponding to the renal cavities is much less active

The comparative value of intravenous urography and DMSA scintigraphy for the detection of reflux nephropathy is no longer a matter of debate. Almost all paediatric urologists and nephrologists require normal DMSA scintigraphy to declare a kidney normal in the presence of vesico-ureteric reflux; it is obvious that in refluxing kidneys, DMSA regional impairment is often observed in the absence of any structural change on X-ray (Verber et al. 1988; Verber and Meller 1989; Whitear et al. 1990). The left-to-right DMSA ratio is a highly reproducible parameter, easy to perform, and is normally in the range between 80 and 120%. Slight background correction is applied using the regions just below and above the kidneys. Children with abnormally low differential function (<45%) on DMSA scan had a scar on intravenous urography (IVU) in more than 95% (Piepsz et al. 1990). Absolute quantification of DMSA uptake (in percent of the injected dose) is used by some authors (Gordon et al. 1987) but needs very careful standardization. Although it is well known that uptake increases during the first few years of life, normal values as a function of age are not available. Finally, care should be taken when using DMSA in cases of hydronephrosis. Urinary activity may significantly interfere with the activity taken up by the tubular cells, giving rise to artefactual images and counting rates (Verboven et al. 1987). Some authors have solved this problem by using delayed 24-h images (De Maeyer et al. 1982).

^{99m}Tc-DTPA is largely used in children with a uropathy for the evaluation of the separate left and right glomerular filtration rate (GFR), as well as for the evaluation of both transit time and drainage. Several algorithms allowing the measurement of GFR for each kidney by means of the gamma camera have been published. Some are rather sophisticated methods based on the corrected renal curve and the plasma curve derived from the cardiac curve, calibrated or not by means of plasma samples (Piepsz et al. 1977; Delcourt et al. 1985; Russel et al. 1985; Rutland 1985). The errors in these methods are mainly related to the interference by the high background observed with diethylene triamine penta-acetic acid (DTPA), particularly in the young age group with low normal clearance values (see neonate section), and to the approximation of the heart curve to a plasma curve. A simplified method based on renal counts during the first minutes expressed as a percent of the injected dose is also used (Gates 1983). The same errors due to background interference may be expected, and additional difficulties arise from the transformation of counts (percent of dose) into milliliters per minute. The algorithm of transformation might be different for different age groups. Others simply calculate the relative left-to-right ratio by external measurements with adjustment to absolute values by means of some simplification of the double exponential analysis of the plasma disappearance curve, using one or several blood samples (Tamminen et al. 1978; Rehling et al. 1985). Although these simplifications have proved to be accurate in adults, their physiological significance is questionable and they still have to be validated for young age groups. Despite these difficulties, estimation of the parenchymal function of each kidney constitutes an essential parameter in the follow-up of paediatric uropathy, and more effort should be made to standardize the technology and assess the normal values in young age groups.

Besides the clearance calculations, the second purpose of DTPA is the evaluation of the transit time for the diagnosis of obstruction. Renal transit times, either derived from the renographic curves or obtained by the techniques of deconvolution (Diffey et al. 1976), can discriminate between normal kidneys and hydronephrosis, but are unable to separate obstruction from simple dilatation (Piepsz et al. 1982). The determination of cortical transit using regions of interest or parametric images (Britton et al. 1979) constitutes progress since a normal cortical transit time allows severe obstruction to be excluded. In children, however, pelvic dilatation, even years after surgical correction, generally does not allow any firm conclusion, owing to the significant overlap of the renal cavities completely masking the renal cortex (Vivian et al. 1984; Verboven et al. 1988). Diuretic renography is theoretically a simple and well-standardized technique (O'Reilly 1986); differences in the way the technique is used may obviously influence the interpretation of the test: the time of furosemide injection, 20 min after or 15 min before tracer injection; the type of tracer used (the quality of the response to furosemide is influenced by the extraction rate of the tracer); the level of hydration of the patient and the parameter chosen to define the time activity curve.

In children, attention should be paid to two pitfalls. The first one is related to the fact that it is mandatory to end the test with an empty bladder (Fig. 3): a full bladder can invalidate the result, giving rise to a false "non-response". Some authors systematically place an indwelling bladder catheter when performing the test (Majd 1984); others try to avoid this supplementary invasive procedure by taking post-voiding images, which can easily be quantified by comparing them to the pre-voiding images (Piepsz et al. 1982; Gordon et al. 1988). The second pitfall is related to the unresponsiveness of immature kidneys to the injection of furosemide: no response or an incomplete response is often observed under 6 months of age. When the same child is examined at an older age without any change in the clinical situation, there may be a satisfactory response. Diuretic renography has also been proposed to assess ureteral emptying in the case of megaureter. The same drawbacks that pertain to renal emptying should be taken into account, however. Moreover, a dilated non-obstructed ureter may simply accumulate some activity, resulting from increased renal emptying.

Finally, it should be emphasized that no matter which radionuclide parameter is used to define obstruction, there is no possibility of predicting recoverability if surgery is undertaken or, in contrast, predicting fur-

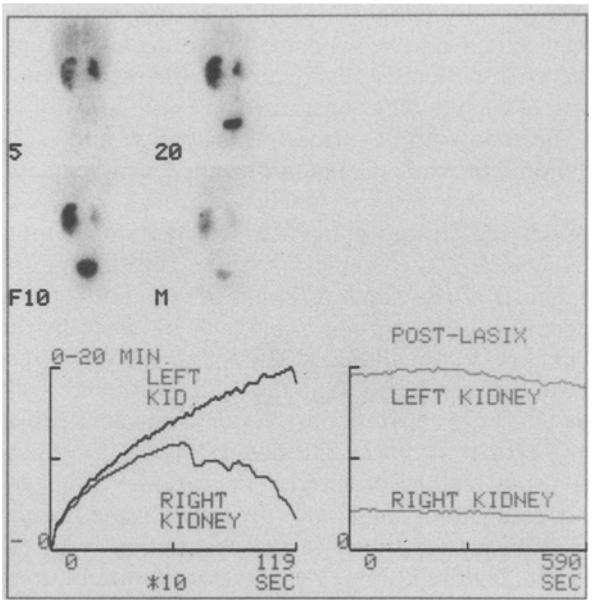

Fig. 3. Dynamic diuertic DTPA scan in a 6-year-old boy 12 months following a left pyeloplasty for a PUJ obstruction. The images in the *top left-hand corner* show good function of both kidneys at 5 min. At 20 min, there is good drainage from the normal right kidney with progressive accumulation of isotope in the dilated left renal pelvis. F10 represents the image 10 min after the injection of Frusemide. There has been no drainage from the renal pelvis. This is reflective in the very flat renal curve seen on the bottom right. The image labelled *M* represents the post micturition image taken 20 min after the diuretic and 40 min after the beginning of the study. This shows an empty bladder and also the left renal pelvis has drained completely. This illustrates the importance of achieving complete bladder emptying before diagnosis a PUJ obstruction

ther deterioration if conservative management is followed (Bratt et al. 1977; Djurhuus et al. 1987; Piepsz et al. 1989).

^{123}I-hippurate is chosen in certain centres instead of ^{99m}Tc-DTPA for the determination of the input and output function of the kidney. The great advantage of this tracer is the higher extraction rate, which consequently improves the signal-to-noise ratio, the accuracy of the left-to-right renal uptake ratio and the response to furosemide. The main drawback of the tracer, besides the fact that it explores a composite function (the tracer is mainly secreted by the tubular cell, but is also partially filtrated by the glomerulus), is that it is expensive and not generally available on a daily basis.

^{99m}Tc-mercaptoacetyltriglycine 3 (MAG3) has become popular recently, but the mechanism of tubular secretion is not completely understood. It combines the advantages of an easily available technetium compound and a high extraction rate, which is lower, however, than the hippurate extraction rate. Although several papers have been published on the methodology of clearance measurement in adults by means of blood samples, work is required to assess the value of this method in children and in evaluating the feasibility of gamma camera methods for separate renal clearance in children and in adults.

Direct radionuclide cystography is more sensitive than X-ray cystography, since the entire procedure of bladder filling and emptying can be recorded. Moreover, the radiation dose to the gonads is considerably lower. Direct cystography requires adequate filling of the bladder; charts have been published giving the filling volumes that can usually be reached in relation to age (Willi and Treves 1985). The small child is examined while lying in a supine position on the gamma camera, which is adequately protected for contamination; the older child is in semirecumbent position with its back against the gamma camera; the tracer is either mixed with the saline or is directly injected through the catheter. The volume of filling at which reflux occurs is noted, although the correlation between this volume and the further spontaneous disappearance of reflux has still to be demonstrated. In recent years, indirect cystography after intravenous injection of ^{99m}Tc-DTPA has been advocated (Pollet et al. 1981; Bower et al. 1985; Carlsen et al. 1986; Chapman et al. 1988; Gordon 1989; Gordon et al. 1990; Peters et al. 1990). The great advantage of this technique is that an indwelling catheter can be avoided. The drawbacks are related to the fact that the bladder filling is incomplete and the kidneys are often not completely empty even 2 h after injection of the tracer. Moreover, cooperation of the child is required, and the technique is more suitable for children over 3 or 4 years of age. However, tracers with higher renal extraction, like hippurate or MAG3 might improve the accuracy of the method considerably (Fig. 4). Moreover, it may include measurement of urine flow patterns and the index of urine transport as a method of screening lower urinary tract function (Van der Vis-Melsen 1988, 1989).

Bone

The first radionuclide used for bone scintigraphy was strontium 85. The long half-life and therefore high exposure to radiation made it strictly limited in application in children in contrast to adults (Tefft 1971). The use of ^{87}Sr (Charkes et al. 1964) and fluorine 18 (Blau et al. 1962) was restricted to a few centres (Samuels 1973) because of the technical problems in handling these radionuclides. With the introduction in 1971 of phosphate compounds labelled with ^{99m}Tc (Subramanian et al. 1971), bone scintigraphy gained significant clinical relevance in paediatrics.

The uptake of technetium-phosphate complexes is dependent on bone metabolism, which in most pathological bone processes is increased. ^{99m}Tc-phosphate complexes have no toxic effect on growth or bone metabolism. In the bone scintigram of a healthy child, the main activity is found in the growth zones (physes) of the extremities and in the parts of bones with predominantly

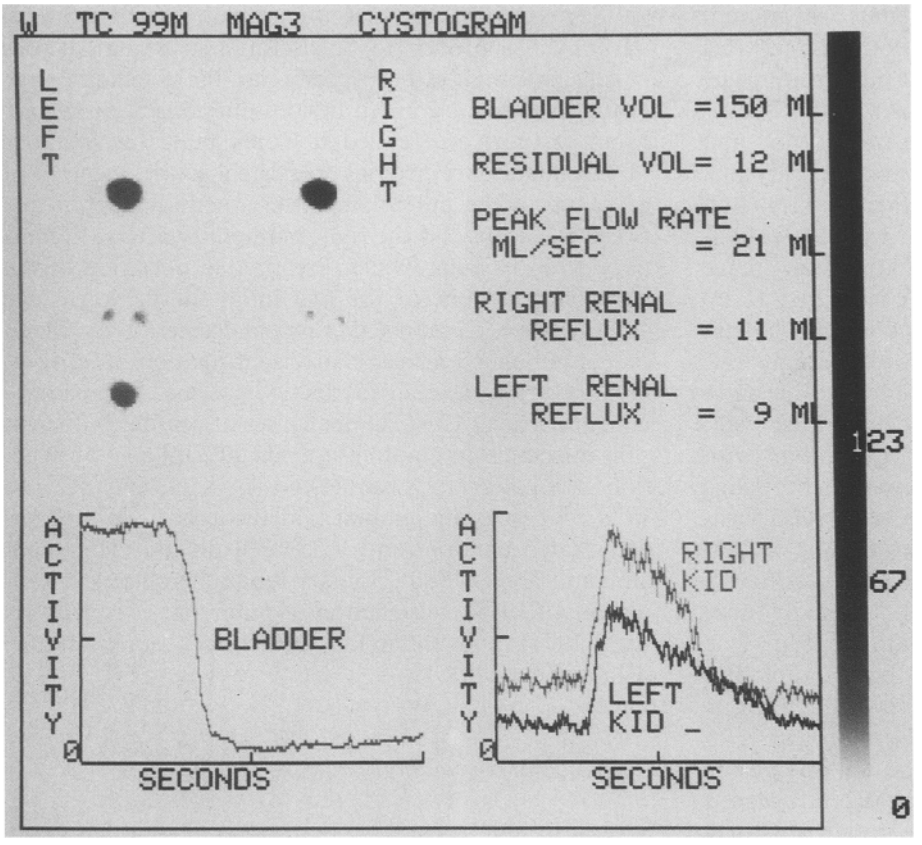

Fig. 4. Indirect radionuclide cystography using ^{99m}Tc-MAG 3. The images on the *top left* show the full bladder with p63 without evidence of any isotope in the kidneys. The lower kidneys reveal isotope in both kidneys. The renal curves clearly demonstrate increased activity in both kidneys, greater on the right than the left. Measuring the urine volume and activity, quantification of bladder volume, residual volume and peak urine flow rate is possible as is quantification of the degree of reflux

spongioid structures. Good knowledge of the position and shape of the physes and the commonly seen developmental variants is necessary to avoid misdiagnosis in the child (Guillet et al. 1982). The Paediatric Task Group of EANM is preparing an atlas of the normal growing skeleton and its variants in relation to age. This is expected to be available at the end of 1991.

Special preparation of the child is not necessary. However, it is usual to encourage hydration by offering the children extra fluids. This results in frequent emptying of the bladder and will reduce the radiation burden since 40% of the injected radioactive dose is eliminated by the kidneys in the first 4 h.

Recent improvement in technical equipment (especially high-resolution gamma cameras and collimators) has resulted in the ability to obtain detailed scans from small parts of the bones and joints. Nevertheless, the use of pin-hole collimators is still required – for instance, to obtain a picture of a child's hip joint (Paul et al. 1974; Ash et al. 1975). SPET systems in older children allow improved localization of the pathological findings (Collier et al. 1987; Weber 1988). This has proved to be especially helpful in the spine and skull, as well as for differentiation between soft tissue and bone abnormalities.

Immediately after the injection of the radiopharmaceutical, sequential images, centered on the concerned area, are taken at 2 s/image for up to 60 s. This first phase allows analysis of the arterial perfusion of bone or soft-tissue processes.

At the end of the dynamic acquisition, single static images with an acquisition time of 2–3 min are taken of the appropriate parts of the skeleton. The images offer information about the arterial and venous blood flow as well as beginning bone metabolism.

Two to four hours after the injection, the delayed images of the skeleton are obtained in at least two views. Older children may be scanned from anterior and posterior positions. Babies and small children lie directly on the head of the gamma camera for the examination.

Lung

Regional lung function can only be assessed using radionuclides. Since consistency is required to compare different children's scans and the same child's sequential examinations, scans should be carried out in a similar manner for all ages. For this reason injection and scan are always carried out in the supine posture. A full series of images includes a posterior, right and left posterior oblique view and an anterior view (Gordon et al. 1981). There is little point in doing lateral images since there is significant "shine through" from the opposite lung during acquisition.

Perfusion studies are not dissimilar to those carried

out in adults using ^{99m}Tc-macroaggregates. The amount of isotope injected is scaled down on a body-surface-area basis. Ventilation scans can be carried out without any cooperation from the child if krypton 81m (^{81m}Kr) is used. All other isotopes require active cooperation and therefore are difficult to use in a child under 5 years. Yet in children under 5 years old, routine lung function tests are impossible to carry out. ^{81m}Kr with a 13-s half-life, offers many advantages in paediatrics: an image readily comparable to the ^{99m}Tc-MAA scan, easy to repeat; no cooperation required; physiological changes can be monitored; the radiation dose is exceedingly low. One potential disadvantage lies in the short half-life since it has been suggested that in the infant with a high respiratory turnover, ^{81m}Kr may get into equilibrium with the air in the alveolar space and therefore the image produced in those children with a high ventilation turnover may reflect lung volume rather than specific ventilation. Another difficulty may be related to the difficulty in accepting a face mask. Many children, especially those under 5 years, hate having a face mask applied. One answer is to keep the mask firmly on the mandible but leave a space around the nose since air-tight fitting is not required for ^{81}Kr. Another useful approach is to discard the face mask and simply thread the fine plastic tube through the operator's hand, which is gently placed on the mandible. This is not frightening and is usually acceptable to the child.

The effect on posture on both ventilation and perfusion has been recognized for a long time. In the adult, the lung that is in the dependent (or down) position is better perfused and ventilated than the upper lung. This is true for both healthy and diseased lungs. In children, however, the dependent lung remains better perfused, but it is the upper lung which is better ventilated. This has practical importance when dealing with children with unilateral lung disease, since placing these children with the diseased lung uppermost may prevent adequate ventilation of the good lung, which is now dependent (Heaf et al. 1983; Davies et al. 1985).

Children with air trapping on the chest radiograph may well demonstrate the phenomena of "turn on – turn off". In this situation the ventilation to a lobe may be seen on one view using ^{81m}Kr, but not on a second view, and yet reappear on the third view (Peters et al. 1989). This phenomenon has been ascribed to the critical changes of ventilation depending on posture. Yet one must recall that the perfusion image represents what was happening at the time of the injection while the ^{81m}Kr ventilation image reflects minute ventilation during the actual image acquisition. The result may be that there is an apparent mismatching of ventilation and perfusion on some views and not on others.

Xenon is used for ventilation, the advantage being that it is readily available. The disadvantage lies in the relatively larger radiation dose to the child and it is not possible to obtain the same four views to compare the ventilation to perfusion.

The combined use of ventilation and perfusion scintigraphy has proven to be useful since several causes of mismatching rather specific to the paediatric age group have been reported besides pulmonary embolism. Most of them are related to congenital abnormalities of the pulmonary arterial tree: stenosis or agenesis of a branch of the pulmonary artery, communication between the aorta and the right pulmonary artery, pulmonary arteriovenous fistula. Preferential deviation of the blood flow to one of the two lungs following cardiac surgery has been reported: surgical correction by Glenn or Fontan anastomosis, inadvertent ligation of left pulmonary artery instead of ductus arteriosus (Papanicolaou and Treves 1980). Other causes of ventilation-perfusion mismatch in children are: distal capillary obstruction secondary to histoplasmosis (Kim and Deland 1978), fat or septic emboli and thrombosis in severely dehydrated children and sickle cell disease (Papanicolaou and Treves 1980), primary lung tuberculosis (Chanoine et al. 1988), obstruction of pulmonary veins (Warkany 1971), and anomalous pulmonary venous return (Chanoine et al. 1988).

Gastro-oesophageal motility

Several techniques may be performed in children: oesophageal transit studies, gastro-oesophageal reflux detection, and gastric emptying determination. For oesophageal transit studies, the patient is placed in front of the gamma camera and a 1-min acquisition after a single swallow of tracer diluted in liquid is the commonest technique used. Small children are positioned above the camera and kept immobile during the acquisition time. In order to avoid double swallows, which could create peristaltic artefacts, the amount of liquid in which the tracer is diluted should be adapted to the age: 0.5 ml in infants to 5–10 ml in older children. ^{99m}Tc-sulphur colloid is the commonest tracer used (Guillet et al. 1984; Taillefer and Beauchamp 1984). However, ^{81m}Kr offers several advantages, particularly in children: the ultrashort half-life of the radionuclide reduces the radiation burden to a negligible level. The administered activity may therefore be much higher, providing high-quality images; the test can be repeated as often as necessary, particularly in a young, uncooperative child who may spit out part of the dose. Contamination of the infant or staff with ^{81m}Kr is unimportant and does not prevent repeated swallows immediately. Time activity curves, drawn over various parts of the oesophagus, are often used to describe the transit alterations; parametric images, e.g. mean time images or condensed images (Fig. 5), offer several advantages, increasing the sensitivity of the test or better demonstrating some abnormal peristaltic contractions (Ham et al. 1984, 1985).

The "milk scan" has been used for many years (Fisher et al. 1976) for the detection of gastro-oesophageal reflux (GOR). The level of information provided by this

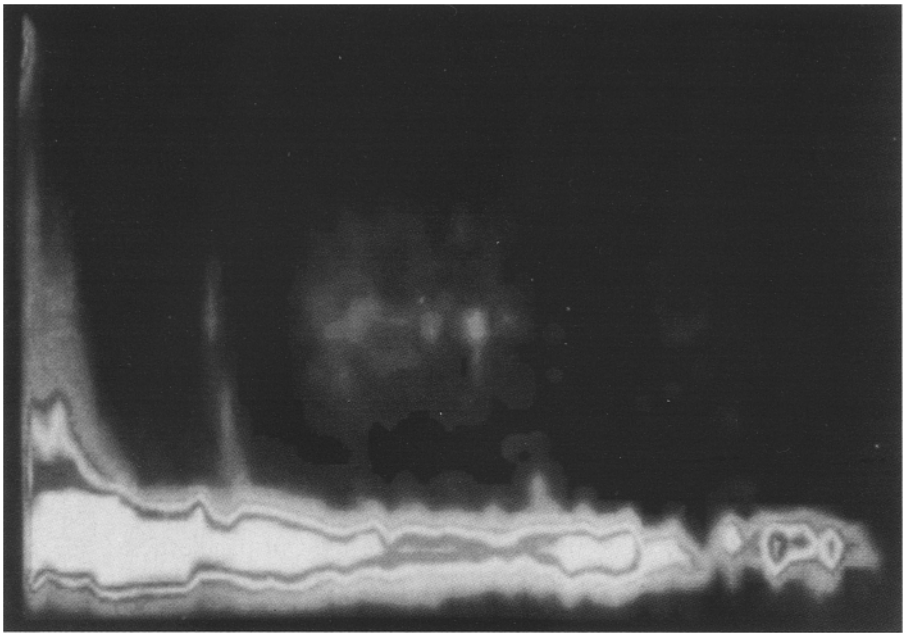

Fig. 5. The sixty 1-s images of a ^{81}m Kr swallowing test are condensed in one single image. *Ordinate*: the oesophageal height from mouth to stomach; *abscissa*: the time in seconds. The tracer passes rapidly from the mouth to the stomach without any delay. A first short episode of gastro-oesophageal reflux is then visualized without any oesophageal stasis of the refluxing material; this is followed by a second episode of reflux, this time with an important transit delay. This constructed image is the best way of representing the various abnormalities of oesophageal peristalsis

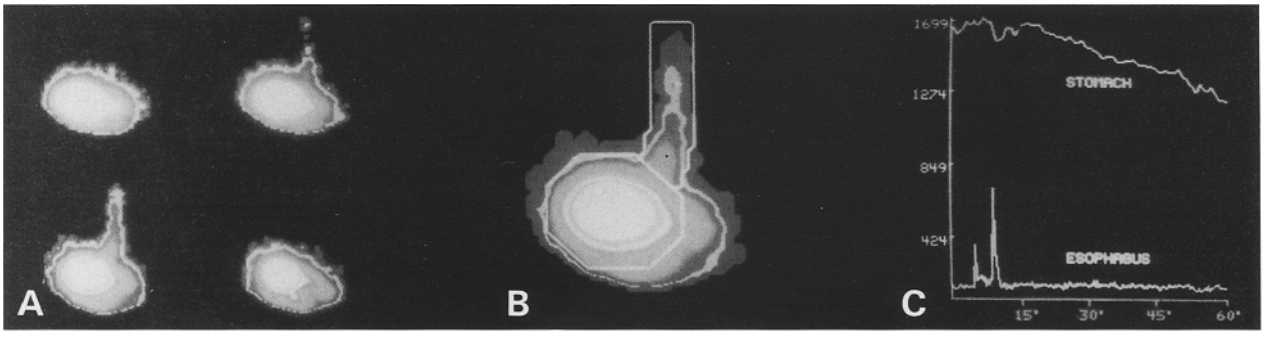

Fig. 6A–C. ^{99m}Tc-sulphur colloid gastro-oesophageal reflux scan. **A** Selected images with enhanced contrast, allowing sufficient visualization of small amounts of GOR reflux. **B** Regions of interest drawn over the stomach and the oesophagus. **C** The upper and the lower curves correspond respectively to the gastric emptying curve and the oesophageal curve. On this last curve, the reflux peaks are easily identified and a reflux index can be estimated, taking into account the number, height and the duration of the reflux peaks

examination is essentially dependent on the quality of the technical conditions of the test. The patient should fast for a minimum of 4 h. The tracer used is ^{99m}Tc-sulphur colloid, which remains stable in the stomach. In a child under 3 years of age, the dose is mixed with a small part of the usual milk formula; pudding can be used in older children. Water, glucose solution or diluted fruit juice is avoided because the gastric transit of these products is too rapid. A nasogastric tube is generally not used in order to preserve the non-invasive character of the test and to avoid any interference with peristalsis. It is important that the mouth and oesophagus should then be rinsed by adding a supplementary amount of non-labelled meal. The supine position on the gamma camera is generally preferred (Heymans et al. 1979; Piepsz et al. 1981) and allows the highest rate for detection of GOR. The recording time is often limited to 30 min, but prolonging this time to 60 min considerably increases the sensitivity of the test.

When inspecting the images, good contrast enhancement should be used in order to allow the detection of refluxing activity as low as 0.5% of the gastric activity. Quantification of the reflux by estimating the frequency, duration and intensity of the reflux peaks may help to evaluate the significance of the reflux (Fig. 6). Time activity curves from a region of interest should be cautiously used because of possible movement artefact by the stomach. Pulmonary aspiration can be detected on delayed images taken over the lung; however, despite some optimistic reports often based on quantification techniques, lung aspiration is seldom observed (Piepsz and Ham 1989), not because of the low sensitivity of the scintigraphic technique, but more likely because the probability is low for such a phenomenon to occur

precisely during the examination. A careful clinical observation of the child during the recording period might be more informative in order to relate the clinical complaints (cough, pallor and apnoea) to the recorded GOR episodes.

Gastric emptying can be measured by means of the gamma camera simultaneously with the detection of GOR, the number of counts over the gastric region of interest being measured. The interpretation of the time-activity curve is, however, not always simple: when milk reaches the stomach, casein precipitates; the radiotracer is more or less sequestrated into this fraction and the gastric emptying time describes mainly the emptying of the casein. In adult patients, the gastric emptying curve generally approximates to a monoexponential and a half-time of emptying has generally been used to define the gastric emptying. Owing to the complex irregular shape of the gastric milk-emptying curve in children, some authors prefer to use the residual activity at the end of the test as the index of gastric emptying. Gastric emptying is essentially dependent on both the age of the patient, older children emptying faster than younger children (Di Lorenzo et al. 1987), and on the type of meal used for the study.

Meckel's diverticulum

The detection of Meckel's diverticulum, using ^{99m}Tc-pertechnetate, is the most reliable technique for making the diagnosis, but depends strongly on the quality of the technical procedure. The patient should fast for about 4 h prior to the study. Barium contrast studies must be avoided for 3–4 days before the scan (the contrast material can cause false-negative results). A nasogastric tube may be useful, allowing continuous aspiration of gastric content to prevent the progress of radioactivity into the small bowel from the stomach, which could produce false-positive images. Oral cimethidine can be used and therefore remove the need for a nasogastric tube. Subcutaneous injection of pentagastrin has been proposed, at a dose of 6 μg/kg body weight, 15 min before the injection of the tracer in order to increase the gastric uptake of pertechnetate anion (Sfakianakis and Conway 1981). Repeated images during a 1-h recording are useful. The abnormal area of uptake due to ectopic gastric mucosa is generally small and its activity intense. It can be located anywhere in the abdomen and appears at the same time as the stomach, following the same time course. The lesion can be confused with a kidney or ureteral dilatation; lateral views may help distinguish. Several other conditions in the abdomen can accumulate pertechnetate (Sfakianakis and Conway 1981), but the images have a different appearance than in Meckel's diverticulum. False-negative results may be due to several causes: too small amounts of gastric mucosa; hypofunction due to necrosis or ischaemia; previous administration of perchlorate. Finally, acute bleeding at the moment of the scan can produce dilution or washout of radioactivity.

Infection/inflammation

In paediatrics, the child with pyrexia of unknown origin causes as much difficulty as in adults. The possible isotopes include ^{99m}Tc-hexamethylpropylene amine oxime (HMPAO) white blood cells (WBC), ^{67}Ga-citrate and ^{111}Indium-labelled WBC. There are also a range of antibodies that are becoming available, and therefore this is an expanding area in nuclear medicine. The use of a small molecule, e.g. a small colloid, has also been suggested. In paediatrics it is possible to undertake labelled WBC in small volumes of whole blood, but the very high radiation burden with ^{111}In suggests that this isotope should rarely be used in paediatrics. ^{67}Ga has the disadvantage of being excreted by the bowel, and therefore the reliability of diagnosing intra-abdominal sepsis is reduced. As in adults, delayed images at 24 and 48 h are essential; the value of 72-h images is uncertain, although these images are routinely carried out.

In the post-operative situation, the use of ^{99m}Tc-HMPAO-labelled WBC are of great value, especially following abdominal surgery (Fig. 7). When there is a long history of illness (months rather than days or weeks), then ^{99m}Tc-HMPAO-labelled WBC scans have been unable to help the clinician despite the presence of chronic

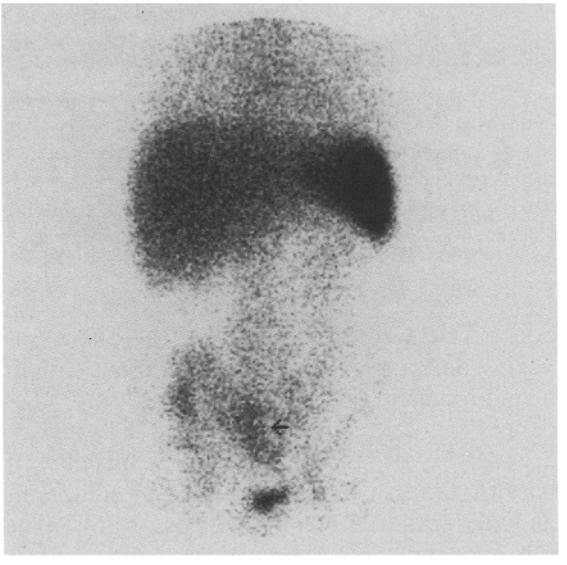

Fig. 7. ^{99m}Tc-HMPAO white blood cell scan. This 4-year-old boy had had recurrent low abdominal pain, fever and weight loss over the previous 6 months. Diarrhoea had also been noted. This image was taken 1 h following the reinjection of labelled white cells using ^{99m}Tc-HMPAO. The isotope is seen in the spleen and, to a lesser extent, in the liver. A little isotope is noted in the bladder. Abnormal accumulation of isotope is noted in the lower right of the abdomen (*arrow*). This child underwent colonoscopy with biopsy and was shown to have inflammatory bowel disease, probably Crohn's disease

infection. In this context, ^{67}Ga may yield more positive results.

In the child with suspected inflammatory bowel disease, ^{111}In-labelled WBC has high sensitivity and specificity, but the high radiation dose prevents this technique from being used even as a second-line examination in paediatrics. Early work suggests that ^{99m}Tc-HMPAO WBC may prove to be as sensitive as ^{111}In WBC, but with a much reduced exposure to radiation.

Thyroid

^{123}I-NaI and ^{99m}Tc-pertechnetate are the two main radiopharmaceuticals used for thyroid scintigraphy. Both have to be injected intravenously. Since ^{123}I is organified in the thyroid gland, it has been advocated as the optimal tracer (Guillet et al. 1981; Hilditch and Jackson 1985), providing better visualization of remnant amounts of thyroid tissue and allowing metabolic studies in case of organification block. ^{99m}Tc-pertechnetate has two major advantages of particular interest in the neonate: the tracer is immediately available and the dosimetry is favourable (Cassio et al. 1984; Ermans et al. 1989). If the neonate is fed between injection of the tracer and the scanning procedure, the result is a quiet child with a reduction of accumulation of tracer in the salivary glands. Profile views may be helpful in localizing better ectopic thyroid tissue. Whether small amounts of thyroid tissue, not visualized on a good-quality ^{99m}Tc image, could be detected by means of ^{123}I, still has to be demonstrated. The theoretical advantage of ^{123}I allowing metabolic studies, does not interfere with neither the strategy of diagnosis and treatment or with evaluation of the prognosis.

Central nervous system

In the recent past, regional brain blood-flow studies with ^{123}I amphetamines or ^{99m}Tc-HMPAO have gained much popularity in all kinds of diseases in adults. In children, however, although this examination has provided interesting information in epilepsy, in high-risk neonates, in cerebral palsy and in dysphasia (Denays et al. 1988, 1989, 1990), the number of studies available is rather limited and the exact suitability of this procedure still has to be determined.

The difficulties in performing this test in children are three-fold:

1. The examination requires complete immobilization for 20 min minimum. Small transitory movement may remain undetected during acquisition, but can produce serious artefacts in the reconstructed images. Several devices can be used to immobilize the head; this is easily achieved in infants, but not always in older children, particularly those between 9 months and 3 years, and sedation might be required in those children. One should remember that drug sedation, as well as the brain stimulation occurring in an agitated and anxious child, might interfere with the regional distribution of the activity in the brain.
2. The distribution patterns of the blood-flow tracers depend on the age of the child. While in the premature infant, the activity is essentially localized in the central parts of the brain (Fig. 8), it moves progressively to the parietal, the occipital and finally the frontal area around 6 months of age (Rubinstein et al. 1989).
3. It seems that the criteria of left-to-right asymmetry are not different in children or adults. However, the detection of an asymmetry is still a delicate matter, since the measurements are not absolute values and each centre has to determine the limits of asymmetry that can be tolerated for a given patient.

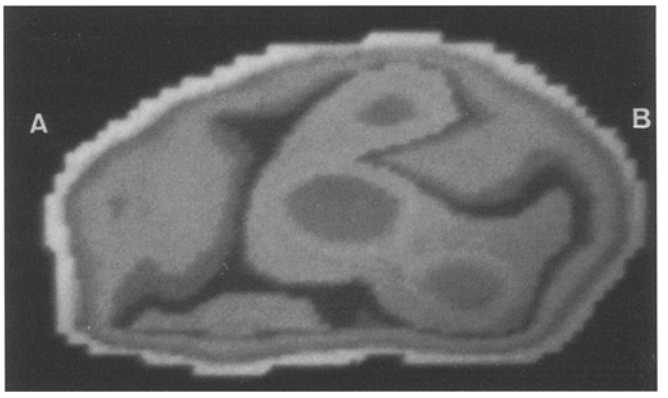

Fig. 8A, B. ^{99m}Tc-HMPAO SPET study in the neonatal period (**A** anterior; **B** posterior); midsagittal slice. Prominent activity in the central part of the brain; lower activity in the parietal region; poor occipital and frontal visualization

Heart

Radionuclide examinations of the heart only have a limited place in paediatric nuclear medicine. Coronary disease and heart failure due to systemic hypertension, which constitute the main indications of radioisotopic studies in adults, are seldom encountered in childhood. Although heart failure is not uncommon in chronic lung disease associated with cystic fibrosis in childhood, the literature devoted to this subject is rather poor compared to the impressive literature on the right heart function in adults with chronic pulmonary disease of long duration. Moreover, bidimensional echography and Doppler flow studies have improved considerably and are now, in the hands of the paediatric cardiologists, an important tool in the investigation of congenital and acquired diseases; they have replaced invasive techniques like cardiac catheterization and inaccurate radionuclide techniques.

Studies of the contractility of the left and right heart using labelled albumin or ultrashort-life isotopes, studies of myocardial perfusion with thallium or MIBI are still

used in children in very specific conditions (Finley et al. 1978; Chipps et al. 1979; Rabinovitch et al. 1979, 1981; Treves et al. 1979; Matthay et al. 1980; Kato et al. 1982; Rajfer et al. 1982; Piepsz et al. 1987). Except for small details, the procedure in these tests is no different in children or adults.

Quantitative radionuclide angiocardiography can still be considered to be a particularly useful and non-invasive technique for the detection and quantification of left-to-right cardiac shunt (Maltz et al. 1973; Alderson et al. 1975) and requires an additional technical explanation. The most widely accepted method consists in the recording of a first pass through the lung and determination of the pulmonary-to-systemic flow ratio (QP/QS) using a gamma-function fit (De Graaf et al. 1976). Although the technique only requires intravenous injection of the tracer and a 60-s recording period, some precautions are needed. The tracer should be injected rapidly as a small bolus, followed by a saline flush according to the technique described by Lane et al. (1972). The child should be quiet and, for that reason, the insertion of the needle into the vein should be separate from the tracer injection in small children; the stress and crying might well induce a transitory increase in pulmonary vascular resistance, resulting in a decrease of a shunt that would be present under resting conditions. The frame rate should be short (0.2–0.4 s) and adapted to the age. It is well known that the circulation time in infants is much shorter than in adults (Siver et al. 1973). The quality of the bolus is essential in the procedure. A small region of interest can be drawn in the midregion of the superior vena cava. If the bolus is fragmented, one cannot expect to be able to interpret the pulmonary curve properly. Unfortunately, despite all precautions, prolonged or double-peak boluses are still encountered in about 20% of the patients. Another delicate point is the outlining of an area of interest over each lung: to avoid superimposition with the heart or the pulmonary artery, parametric images, as described by Goris et al. (1976), may be useful in children. Finally, in the case of prolonged bolus, it has been shown that deconvolution analysis of the pulmonary curve can considerably improve the results, giving better separation of pulmonary, shunt and recirculation curves (Alderson et al. 1979; Ham et al. 1981).

Maturation in infancy

The neonate is almost as different from the child as the child is different from the adult. This is best seen in the kidney, brain and lung.

Kidney

Transitional nephrology refers both to the adaptation of the fetus to the external environment and the maturation of the kidney. The ratio of intravascular space to extravascular space is important when considering isotopes that are freely diffusible, e.g. DTPA. In the infant there is a relatively large extravascular space so that any freely diffusible substance injected will have a low plasma concentration in the infant – this is most marked in the neonate compared to the older child. The GFR is very low at birth (20–40 ml/min/1.73 m^2), rising by the end of the neonatal period to 40–60 ml/min/1.73 m^2. By the end of the second year of life the GFR has reached 80%–90% of the adult value (Aperia et al. 1981). The tubules are even more immature than the glomerulus at birth, but the maturation of the tubules is more rapid than the glomerulus, reaching 80%–90% of adult maturity by the end of the first year of life (Strauss et al. 1981).

These physiological factors explain why ^{99m}Tc-DTPA scans in the neonate are characterized by poor visualization of the kidneys, a high background with a low signal-to-noise ratio and yet a rapid transit time through the kidney. Any renal pathology examined in the early neonatal period and again in early infancy will show improvement simply because of renal maturation. This may well explain some of the so-called excellent results of early surgery in those children with an antenatal diagnosis of renal pelvic dilatation since similar results are now seen in those neonates left untreated early on. Using ^{99m}Tc-MAG3, the relatively high protein binding allows less isotope to pass into the extravascular space and therefore more isotope is presented to the kidney. This, coupled with the greater extraction efficiency of ^{99m}Tc-MAG3 compared to DTPA, results in better renal delineation and higher signal-to-noise ratio. There may well be a more reproducible differential function in the neonatal period using ^{99m}Tc-MAG3.

With ^{99m}Tc-DMSA, the tubular immaturity results in poor uptake of the isotope with a consequent high urinary concentration, as well as a high background level of ^{99m}Tc-DMSA. If a renal scar is to be excluded, a ^{99m}Tc-DMSA scan should not be done before 12 weeks of age. To distinguish between a non-functioning kidney and a poorly functioning kidney, a ^{99m}Tc-DMSA scan may be carried out much earlier, including during the neonatal period.

Lung

The use of ^{81m}Kr for ventilation images may have disadvantages in the neonate. The theoretical basis for this concern comes from the work of Fazio and Jones (1975), who suggested that the short half-life of ^{81m}Kr (13 s) would never allow the isotope to reach equilibrium in the alveolar spaces and, therefore, the ^{81m}Kr image would reflect specific ventilation. This theory was based on a minute ventilation of 3 l. However, at higher specific ventilation, as seen in the neonate, especially the sick neonate, Fazio and Jones (1975) suggest that ^{81m}Kr may

reach equilibrium in the alveolar spaces and therefore the ^{81}Kr image would reflect volume rather than specific ventilation. This theory is supported by the work of Ciofetta et al. (1980). However, recent unpublished work (Davies, personal communication) suggests that even with a minute ventilation of up to 13 l/min, the ^{81m}Kr image may represent specific ventilation and not volume. Where ^{81m}Kr scans are carried out in neonates, it has been noted occasionally that segmental defects in ventilation may be seen, suggesting that the ^{81m}Kr image represents specific ventilation rather than volume. This finding is not universal and some young infants with segmental lung disease have not shown any segmental abnormality. This area requires further work to understand which pathophysiological processes will show defects and which will not.

Brain

In the neonate, the interpretation of SPET images using blood-flow tracers is not easy due to the fact that the activity accumulates mainly in the central part of the brain, with only slight activity in the cortical area (cf. central nervous system).

Nuclear medicine in the strategy of paediatric diagnosis and management

It is unrealistic, even in an extensive review paper, to cover all the areas of application of nuclear medicine in paediatrics. A few select topics have been chosen since the specific paediatric applications are apparent and to underline the place of nuclear medicine compared with other diagnostic procedures.

Urinary tract infection

Infection of the urinary tract (UTI) has several clinical subgroups, each requiring different degrees of investigation. The most severe, acute pyelonephritis, is characterized by ill health, anorexia, pyrexia ($>38.5°$ C), an erythrocyte sedimentation rate >20 mm/h or C-reactive protein >10 mg/l, pyuria, bacteriuria and possible septicaemia. The child may well require hospitalization and parenteral antibiotics. The term "cystitis" is used to refer to those children with lower urinary tract symptoms but without systemic illness who have more than 100,000 bacteria/ml in the urine. They should be distinguished from those children who are asymptomatic but nevertheless have positive urine cultures, i.e. asymptomatic bacteriuria. This last group is usually composed of girls over 5 years of age who do not require much investigation. Clinically, these three groups overlap to some extent, but nevertheless the presentation should be a guide to the choice of the appropriate imaging.

Clinical context. A prospective study by Dixon (1979) found 3.1/1000 girls and 1.7/1000 boys presented annually with their first symptomatic UTI. The incidence of end-stage renal failure due to pyelonephritis in Europe in individuals <40 years of age is 4–5 per million per year. Combining various data, Haycock (1986) estimated the risk of renal failure due to reflux nephropathy in children presenting with UTI as $<1\%$ for boys and $<0.5\%$ for girls. In part, this risk arises from pyelonephritic scarring as a result of to UTI and in part from renal dysplasia associated with VUR. The probability that any child presenting with UTI is at risk from preventable renal failure is thus less than Haycock's estimate, perhaps 6 out of a million. Renal damage may result when UTI occurs either in the presence of obstruction or, under certain conditions, when VUR is present. Scarring in association with VUR appears to depend on a number of factors: infection, intrarenal reflux and age, the young, especially those <1 year of age being at greatest risk. Scarring in association with VUR is usually apparent at the initial investigation, suggesting that either it occurred with the first UTI or that the appearance is due to dysplasia before the child was first seen (Birmingham Reflux Study 1987). The development of new scars has been described, but is rare, especially in the asymptomatic older child (Sherwood and Whitaker 1984; Smellie et al. 1985).

Clinical controversy. Most clinicians agree that with UTI and VUR the age of the child is an important determinant of the risk of scarring. The kidney of young children (<1 year of age) is most susceptible, while in a child >5 years old with normal kidneys, scarring very rarely develops, especially if the child is asymptomatic. The greatest controversy is about the child between these two age groups: Is VUR the major anomaly to be excluded or should one focus on the kidney? The logic is that if the kidney has not scarred after the first UTI, then it is unlikely to do so later on in this age group, so that the presence or absence of VUR may be unimportant. Verber et al. (1988) and Whyte et al. (1988) have both shown that it is only worthwhile to look for VUR in children with an abnormal kidney in this in-between age group; conversely, there are children in this age group with VUR but without renal scars (White 1989).

Selection of children for imaging. Children of either sex with their first *proved* UTI require imaging, the younger child being especially important to investigate. The studies of Williams (1976) and Dikson (1979) have shown that only 18–24% of children with lower urinary tract symptoms actually have UTI, which suggests that the single most important way to avoid unnecessary investigations is to ensure that only those with a definite UTI are investigated.

Aims of imaging. Firstly, imaging is to diagnose obstructive uropathy. With increasing use of antenatal ultra-

sound, many congenital obstructions are diagnosed in utero. Secondly, it is done to detect the presence of calculi and, thirdly, to identify the children with existing renal damage who are at risk of long-term complications (either hypertension or chronic renal failure). Fourthly, we hope to identify those children who are at risk of developing renal damage and, finally, to monitor progress and the results of surgery.

Imaging controversy. Classically, the diagnosis of renal scarring has been based on the IVU and VUR on contrast MCU. Newer imaging techniques with lower degrees of invasiveness are widely available; their role in this clinical context is being constantly appraised. There is little value in comparing a high-quality IVU with an inadequate abdominal ultrasound examination (US) or ^{99m}Tc-DMSA scan. It is the responsibility of nuclear medicine physician to ensure that good techniques (e.g. radionuclide cystography or ^{99m}Tc-DMSA scanning) do not develop bad reputations because of poor-quality examinations.

US should be used to diagnose all cases of obstructive uropathy, the majority of calculi and the presence of a small kidney. Renal length can be measured accurately by US in the majority of children and longitudinal examinations provide evidence of renal growth. A full US examination includes views of the bladder and the area behind the bladder. Numerous studies have shown the high sensitivity and specificity of US as a screening procedure for children with UTI compared to the IVU (Jaquier et al. 1983; Sherwood and Whitaker 1984; Whyte et al. 1988). If scarring is detected on US, then there is no reason to doubt its existence, but a normal US does not exclude a renal scar.

Recent studies support the early impression of the high sensitivity of the ^{99m}Tc-DMSA in the detection of a renal scar. The initial IVU missed most of the scarring compared to ^{99m}Tc-DMSA in children between 0 and 6 years (Goldraich et al. 1989). This is not surprising, considering that this is the age when it is particularly difficult to obtain a high-quality IVU. Most studies show that the ^{99m}Tc-DMSA scan does have a false-negative rate, but this is low compared to the false-negative rate for the IVU. The time necessary for the development of a renal scar is unclear. Using the IVU, the shortest time recorded is 8–9 months. Using ^{99m}Tc-DMSA, Monsour et al. (1987) showed that 25% of kidneys had photon-deficient areas if scanned during the first month after the UTI, while at 6 months only 4% still had defects that could now be called scars. A similar time course has been seen in experimental UTI in the pig using ^{99m}Tc-DMSA (Parkhouse et al. 1989). However, Verber et al. (1988) found that 80% of all defects seen early on remain unchanged on follow-up ^{99m}Tc-DMSA scan in a selected group of children.

The MCU has been suggested as the first-line imaging investigation in UTI. The information provided is restricted to the bladder, bladder emptying and VUR (Blickman et al. 1985). Renal reflux may be detected using radionuclide cystography with a reduction of radiation exposure by a factor of 20 compared to the MCU (Rothwell et al. 1977). In the toilet-trained child, an indirect radionuclide cystogram (IRC), without the necessity for bladder catheterization, can be carried out using ^{99m}Tc-MAG3. In the younger child (i.e. not toilet trained), a direct radionuclide cystogram (DRC), which requires a bladder catheter (a procedure similar to the classical MCU), may be undertaken.

Imaging protocol. Every child with the first-proved UTI requires a full ultrasound examination. If this is normal and the child is over 5 years of age, further imaging (^{99m}Tc-DMSA scan) is optional. All children under the age of 1 year require both a ^{99m}Tc-DMSA scan to exclude scarring and a cystogram to exclude reflux. In children aged between 1 and 5 years, a ^{99m}Tc-DMSA scan is required; if normal, nothing further should be done but if abnormal, then a cystogram is required. If the presenting ultrasound is abnormal, the imaging will follow the lines suggested by the US (Gordon 1990).

Neonate with hydronephrosis prenatally detected

Prenatal ultrasound has considerably modified the strategy in paediatric uropathy. The diagnosis, previously delayed for years because the child was asymptomatic or because the symptoms were not striking enough to require further investigation, is now established from the very first weeks of life. Moreover, the infant is usually asymptomatic and the question sometimes arises whether any surgical correcting procedure should be undertaken.

Renal ultrasound is performed in the neonatal period as a first imaging procedure. This confirms the renal pelvic dilatation detected in the prenatal period and establishes whether it is unilateral or bilateral. An association with dilated ureters and/or an enlarged bladder is also being sought; other findings include the presence of a small kidney, a multicystic kidney, the possibility of renal scars, or an ureterocele. Ultrasound constitutes the first imaging examination.

Radiological micturating cystourethrography is indicated when the diagnosis of a urethral valve or vesicoureteric reflux (VUR) is suspected. The diagnosis of VUR modifies further imaging since the strategy is to prevent urinary tract infections that could be responsible for renal scarring. Except in particular conditions, surgery for VUR is generally avoided, at least during the first years of life. Repeated ultrasound, radionuclide cystography and radionuclide renal function tests then become mandatory.

Whatever the results of X-ray cystography, the first radionuclide examination to perform in congenital hydronephrosis should take place at the end of the first month of life: the ^{99m}Tc-DTPA study is generally per-

formed no earlier than 1 month because of the low extraction rate of the tracer and the low accuracy of the absolute or relative clearance measurements during the first weeks of age. ^{123}I-hippurate and ^{99m}Tc-MAG3, having a more favourable extraction rate, might provide more accurate clearance results, at least for the left-to-right clearance ratio. The cortical transit determination and the diuretic renography, which are widely used for the diagnosis of obstruction (Britton et al. 1979; O'Reilly 1986), can only exclude the diagnosis, since too many pitfalls are related to abnormal cortical transit or to a failure to respond to furosemide during the first 6 months of life (Kass et al. 1985; Piepsz et al. 1982, 1989). During this period, a low clearance value associated with an abnormal left-to-right ratio is probably an indirectly better index of the severity of the obstruction.

Intravenous urography has a low priority among the imaging techniques to be used in the neonate, because of the poor-quality images and the possible complications due, for instance, to the high osmotic load of the contrast product. Further management is complex. A simple attitude cannot be adopted from the data in the literature. There is an absolute indication for surgery in unequivocal obstruction, e.g. ureterocele or posterior urethral valve, or major infectious complications on hydronephrosis. PUJ obstruction, associated with a poor-functioning kidney, is also an indication for surgery, since one can hope to improve not only the drainage function, but also the parenchymal function (Vihma et al. 1977; Bejjani and Belman 1982; King et al. 1984; Kass et al. 1985; Sukhai et al. 1986). However, several authors have pointed out that recovery of renal function is often not the issue of reconstructive surgery. One should keep in mind that a moderate post-operative increase of renal function can simply be due to the phenomenon of renal maturation occurring during the first 2 years of life (Piepsz et al. 1989). Whether isolated renal pelvic dilatation with normal or slightly altered renal function should be operated on or not remains uncertain. The supporters of the surgical attitude evaluate the risk. on a long-term course, of progressive degradation of renal function. This assumption is, however, at present not supported by the experimental or clinical data which, on the contrary, suggest that in non-operated PUJ obstruction, the parenchymal function can remain unchanged for years (Bratt et al. 1977; Josephson 1983; Piepsz et al. 1989). That means that in these cases, repeated renographic studies seem safer than, for instance, the invasive Whitaker flow studies. Further work is needed on this matter and radioisotopes have a major role to play in clarification of the problem: evaluation of the parenchymal function and of drainage function, before and during any medical or surgical treatment.

The place of ^{99m}Tc-DMSA in the strategy of obstruction is more controversial: the free urinary activity included in the renal area may interfere with the interpretation of the morphological and functional parameters of the 2–4 h images. The use of delayed studies (24 h) has been suggested (Verboven et al. 1987; De Maeyer et al. 1982). DMSA has been used for the evaluation of pre- and post-operative parenchymal function, as well as in the early detection of renal scars in hydronephrosis related to vesicoureteric reflux (Kawamura et al. 1978; Parker et al. 1981).

Renal transplant

In the presence of either poor urine output or deteriorating renal function, the clinician is faced with the need to distinguish between acute tubular necrosis, renal artery or venous thrombosis, obstruction and acute rejection in the early post-transplant period. In the later period cyclosporin toxicity, as well as hypertension due to renal artery stenosis, must also be considered in the differential diagnosis.

The integrated use of both Doppler ultrasound and dynamic renography provides unique information for the clinician. Rapid dynamic acquisition following a bolus injection of ^{99m}Tc-DTPA or MAG3 allows the arterial phase to be analysed and the results presented either as a relative index (Hilson index) or as a percentage of cardiac output (Peters et al. 1987). The transit time index is valuable with DTPA, especially if it is short. The strategy following transplantation is no different in children than in adults.

Hypertension

Sustained non-acute hypertension is better recognized in paediatrics. The more severe the hypertension and the younger the child, the more likely it is to be secondary hypertension. Renal pathology is the cause in over 90% of children over 1 year of age.

Causes. Any abnormal kidney may produce renin and so generate hypertension. While scarring is the commonest abnormality, occasionally PUJ obstruction or Wilms' tumours may present with hypertension. Renovascular disease may also cause renin-dependent hypertension. Phaeochromocytomas, uncommon in childhood, are seen and are frequently both multiple and extra-adrenal in origin (Fig. 9). Essential hypertension is seen, usually in the borderline cases, often with a positive family history of hypertension.

Imaging. US will detect the small kidney, the severely scarred kidney, renal and most adrenal tumours, and significant hydronephrosis. A normal US does not exclude a single renal scar nor a phaeochromocytoma. The ^{99m}Tc-DMSA scan will detect a renal scar. A normal US and normal ^{99m}Tc-DMSA scan do not exclude renovascular disease. The exclusion of renovascular disease ultimately requires angiography, but the use of both ^{99m}Tc-DTPA and DMSA before and after ACE inhibition (captopril stimulation) is currently being evaluated.

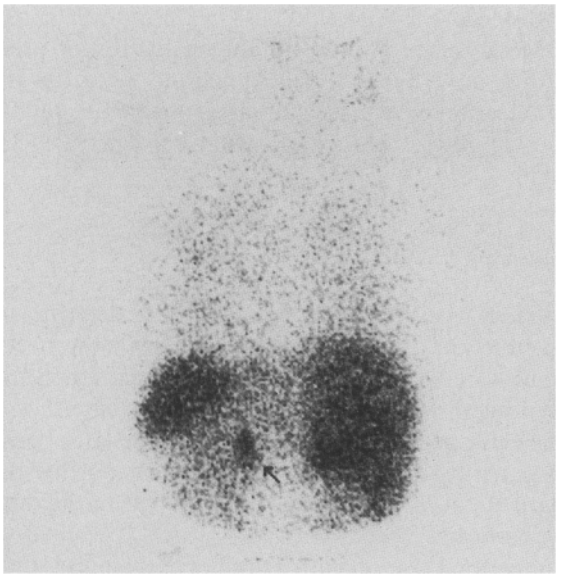

Fig. 9. A 14-year-old with severe headaches and blurring of vision who was found to have hypertension p62. The urinary catecholamines were elevated and the diagnosis of a pheochromocytoma was made. This ^{123}I-MIBG scan shows distribution of the isotope in the liver and spleen with a little activity in the lungs. Abnormal activity is noted in relationship to the left adrenal gland (*arrow*). At surgery a 3 cm pheochromocytoma was removed

Arteriography and selective renal injections are required to exclude both intrarenal and extrarenal renovascular disease. Neurofibromatosis and fibromuscular hyperplasia are probably the two commonest vascular pathologies encountered. If a phaeochromocytoma is suspected both clinically and biochemically, then following the US an iodine metaiodobenzylguanidine (MIBG) scan should be carried out, followed by a CT scan with specific attention focused on the areas of abnormality as seen on the ^{123}-I-MIBG scan.

Recurrent chest infection

Recurrent lung disease is a major cause of admission to the paediatric ward. Clinical history, physical examination, sweat test, allergic skin tests, tuberculin sensitivity, blood sampling, and a chest X-ray constitute the first-line examinations for assessing the diagnosis of allergic disease, immunological deficiency, cystic fibrosis, congenital or acquired lung malformation, tuberculosis or heart disease.

Foreign-body inhalation is a common cause of recurrent lung infection in young children. The condition is often misdiagnosed because the child's parents may fail to recognize the episode of inhalation. Chest X-ray may reveal either an area of consolidation or air trapping, which should alert the physician. Sometimes, because the lesions are not obvious, the X-ray may falsely be interpreted as normal. Lung scintigraphy (ventilation as well as perfusion scintigraphy) generally shows an unequivocal marked segmental or lobar hypoactivity, which helps the physician in making the decision for endoscopy (Leonidas et al. 1973; Mussa et al. 1981). Following foreign-body extraction, there is usually spontaneous recovery of lung function, when the diagnosis and treatment have been made within the 6 weeks following the inhalation (Rothman and Boeckman 1980; Farber 1981). Foreign-body inhalation may be responsible for chronic lesions such as granulomas or bronchiectasis. Lung scintigraphy (Fig. 10) plays a major role in detecting persistent lesions (Guillet et al. 1983; Khiati et al. 1984; Piepsz 1988).

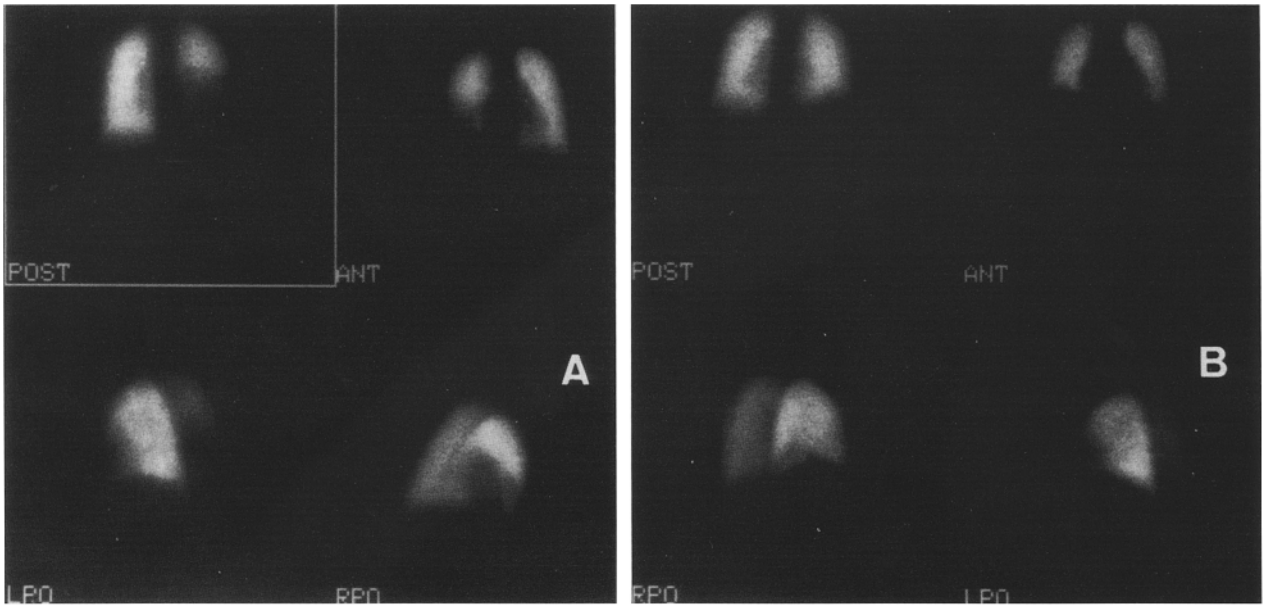

Fig. 10A, B. ^{99m}Tc-MAA perfusion lung scintigraphy: inhalation of a foreign body in a 4-year-old child. **A** Before removal of the foreign body, the right lower and middle lobes are not visualized. **B** Four months after removal: striking improvement; severe defects are nevertheless observed in the right lower lobe. The chest X-ray is normal at that time

Bronchiectasis is generally the consequence of acquired bacterial or viral lung infection and is responsible for recurrent lung disease. The diagnosis is definitely made by bronchography, obtained after intrabronchial instillation of contrast. However, the method is invasive and can give rise to local complications. Moreover, the examination should not be performed following a recent acute infectious episode since irregular contours of the bronchial walls are often observed in the weeks following an acute infection, and this could be misleading for irreversible bronchiectasis. The clinical picture of bronchiectasis is often non-specific, and it is unthinkable to submit every patient with recurrent lung disease to this invasive procedure.

Chest X-ray may show chronic consolidation or abnormal thickening of the bronchial wall. These findings are, however, neither sensitive nor specific; chest X-ray can be normal in one-third of the patients with proven bronchiectasis. Lung scintigraphy (both ventilation and perfusion studies show perfectly matched defects) is a sensitive indicator of segmental poor function leading one to suspect bronchiectasis. V/Q scans should be performed in all cases of recurrent lung disease in childhood (Vandevivere et al. 1980). The combination of normal chest X-ray and lung scintigraphy means that the chance for bronchiectasis is less than 5%. However, lung scintigraphy is non-specific and the diagnosis of bronchiectasis can only be suggested on this basis.

The patient will thereafter generally undergo an intense medical treatment and both examinations, chest X-ray and lung scintigraphy, may be repeated some months later: if the lesion persists with the same localization, the probability of bronchiectasis increases: repeated scintigraphic studies may decrease the number of non-contributive bronchographic examinations. Finally, it is not exceptional that under intensive medical treatment, the scintigraphic defect progressively decreases in size because of the regression of lung infection in the area surrounding a lesion of proven bronchiectasis. This might be important if a surgical decision has to be taken.

Lung scintigraphy is not helpful in the diagnosis of cystic fibrosis. The extension and severity of the regional lung impairment can be more accurately evaluated on lung ventilation or perfusion scintigraphy than on chest X-ray (Fendel and Feine 1970; Samanek et al. 1971; Schnaars et al. 1972; Alderson et al. 1974; Piepsz et al. 1980). On annual studies, the scintigraphic defects are permanent or increase in number and size, and regression is not observed unless the examination has been performed during an acute exacerbation of pulmonary infection.

In primary tuberculosis in childhood, which can sometimes present simply as recurrent lung infection, hilar lymphadenopathy may induce compression of a bronchus that results in ventilation disturbances. Bronchoscopy, which is an invasive examination, can prove bronchial compression. Early recognition of bronchial compression is mandatory in order to evaluate the need for steroids in addition to antituberculous therapy. Persistent ventilation impairment can produce permanent bronchiectatic sequelae, which may be prevented by steroid treatment (Gerbeaux 1967). Although this ventilation impairment is often suggested by standard chest X-ray, scintigraphy may help to identify children requiring bronchoscopy by demonstrating regional defects not suspected on X-ray (Vandevivere et al. 1981; Guillet et al. 1983). Finally, perfusion and ventilation are generally perfectly matched, but in some cases, striking mismatching may be observed, which corresponds probably to an elective tuberculous involvement of the pulmonary artery (Chanoine et al. 1988).

Mismatching, which in adults corresponds generally to pulmonary embolism, can be found in recurrent lung disease in childhood associated with several congenital abnormalities of the pulmonary arterial tree: stenosis or agenesis of a branch of the pulmonary artery, communication between the aorta and the right pulmonary artery, pulmonary vein occlusion and partial anomalous pulmonary venous return (Papanicolaou and Treves 1980; Hartshorne et al. 1985; Chanoine et al. 1988). The presence of a sequestrated lung segment, which has intact bronchial connections but has an arterial supply from the aorta, may show either a matched defect or intact ventilation with loss of perfusion. This condition is more common in the hypoplastic lung.

Gastro-oesophageal reflux is now classically recognized as a cause of recurrent lung disease, even in the absence of any digestive symptom. It has been shown (Malfroot et al. 1987) that GO reflux scan may detect those patients who will improve both GO reflux and recurrent lung disease under intensive antireflux treatment. A GO reflux scan and a 24-h pH study are complementary for that purpose and because the latter examination cannot detect non-acid reflux, it is not unusual that the GO reflux scan is the only technique that allows a correct diagnosis to be made. The procedure will be repeated later on under treatment or when the treatment has been interrupted.

Direct detection of lung aspiration, using delayed thoracic images after GO reflux scintigraphy, has been advocated as an additional advantage of the technique (Boonyaprapra et al. 1980). Several authors, on the other hand, consider that this technique is rarely contributive, even if the patients have been selected on the basis of respiratory symptoms (Heymans et al. 1979; Piepsz et al. 1980). Quantification techniques have been proposed in order to improve the sensitivity of aspiration detection. It is, however, improbable that these techniques will show an abnormal accumulation of tracer in the lung better than a well-contrasted plain image. The low grade of detection of lung aspiration is not due to low sensitivity of the technique but, more likely, to the low probability that an event like pulmonary aspiration occurs during the few hours of the scintigraphic examination.

Finally, one should underline the possible role of

oesophageal transit measurement in the strategy of recurrent lung disease. Marked transit delay and striking antiperistaltic movements may be observed. These alterations may be the consequence of GO reflux and peptic oesophagitis but may be observed in the absence of any GO reflux, suggesting that recurrent lung disease could be directly related to the abnormal oesophageal peristalsis (Wynchank 1988).

Bone tumours

Primary benign and malignant bone tumours or tumour-like lesions, have abnormal bone scans. Thus, there is a role both in diagnosis and staging for bone scans. The tumour, benign or malignant, can be detected in nearly 100% of the cases. Differentiation between a malignant and benign primary bone tumour is rarely possible with nuclear medicine in cases of increased bone metabolism (Schaub and Hahn 1990). Primary malignant bone tumours generally give rise to distinctly increased tracer accumulation (Mc Killop et al. 1981; Rees et al. 1986). Quickly growing juvenile bone cysts and osteoid osteomas can be associated with similar findings (Smith et al. 1980). Lung metastases from osteogenic sarcoma may be detected on bone scans (Siddiqui et al. 1979; Hoefnagel et al. 1981).

Skeletal scintigraphy. Skeletal scintigraphy is recommended in cases of benign bone tumours, especially if the following problems are in question: diagnosis of osteoid osteoma (Smith et al. 1980; Omojola et al. 1981; Schaub et al. 1987); evidence of growth activity of cartilaginous exostosis (Sneppen et al. 1978; Hudson et al. 1983; Lange et al. 1984); expansive bone lesions on radiography to differentiate between aneurysmal bone cysts and a malignant change (Buirsky et al. 1984; Hudson 1984); determination of the activity and expansion in fibrous dysplasia (Fitzer 1977; Doppelfeld et al. 1978); detection of active areas in histiocytosis X (Parker et al. 1980; Crone-Münzebrock and Brassow 1983; Schaub et al. 1983, 1987).

Metastases. Malignant tumours that potentially metastasize to bones are an indication for bone scintigraphy. Scintigrams of the entire skeleton should be performed in the initial work-up (Gilday et al. 1977; McNeil 1984; Sty et al. 1985; Garty et al. 1989). Additional radiographs of any abnormal area are required to exclude incidental pathology, e.g. a fracture or to settle uncertain scintigraphic results. Follow-up bone scans can monitor the course of the disease and/or therapeutic effectiveness.

Osteomyelitis

The course of inflammatory skeletal disease in children depends on rapid diagnosis, early treatment with antibiotics and immobilization. Early diagnosis is difficult since osteomyelitis may progress without any local symptoms in the first few days. Radiological abnormalities of the skeleton do not appear until 10 to 21 days after the beginning of the disease and in young infants a little earlier. Bone scintigraphy is usually abnormal in the presence of osteomyelitis early on (Fig. 11) (Duszynski et al 1975; Maurer et al. 1981; Bressler et al. 1984; Sty et al. 1988; Garty et al. 1989); however, false-negative bone scans have been reported (Ash and Gilday 1980; Gilday 1980; Howie et al. 1983). These negative studies were all based on delayed static images alone rather than on three-phase bone scintigraphy. Nevertheless, great care must be taken, especially in the newborn, when there is a strong clinical suspicion of osteomyelitis and the bone scan is negative (Tröger et al. 1977, 1979; Hahn 1979, 1980, 1985; Hahn et al. 1986).

In the newborn, osteomyelitis leads to vascular compression (Trueta 1975) with subsequent reduced perfusion and therefore reduced accumulation of the radionuclide in the areas of concern (Kemp and Lloyd-Roberts 1974). The result may either be a normal bone scan or a cold lesion may be detected with modern technical equipment, which together with the corresponding clinical findings, suggests osteomyelitis.

In chronic osteomyelitis, the role of isotopes remains uncertain. The ^{99m}Tc-MDP bone scan may remain hot for a significant time, but that may not necessarily reflect active infection. Labelled WBC using either ^{111}In or ^{99m}Tc-HMPAO normally goes to the bone marrow, and therefore the interpretation of the scan is difficult. The use of ^{99m}Tc-colloid for bone-marrow imaging as part of a comprehensive complex of examinations is appealing, but results from the combination of a ^{99m}Tc-MDP and ^{99m}Tc-colloid, as well as a labelled WBC scan in this group of children, is the best approach.

In septic arthritis, bone scintigraphy may be positive earlier than the X-ray. Using the three-phase technique, it may be possible to differentiate arthritis from osteomyelitis (Kloiber et al. 1983; Israel et al. 1987). Bone scintigraphy has been reported as normal in certain cases of acute septic arthritis. The sensitivity of this technique is much lower for septic arthritis than it is for acute osteomyelitis. Caution should therefore be used when suggesting that a bone scan should be undertaken in a child with suspected acute septic arthritis. This is especially true when septic arthritis of the hip is seriously suspected. Then imaging has very little to offer. If the bone scintigraphy is negative or positive, the child must either have needle aspiration or an exploration. Delay in the diagnosis and treatment of septic arthritis of the hip may result in avascular necrosis of the femoral head, and therefore bone scans have no role in primary diagnosis.

Discitis is a condition that is often misdiagnosed. The radiograph can remain negative for weeks, whereas bone scintigraphy generally suggests the correct diagnosis, which will later on be confirmed on CT scan (Wenger et al. 1978).

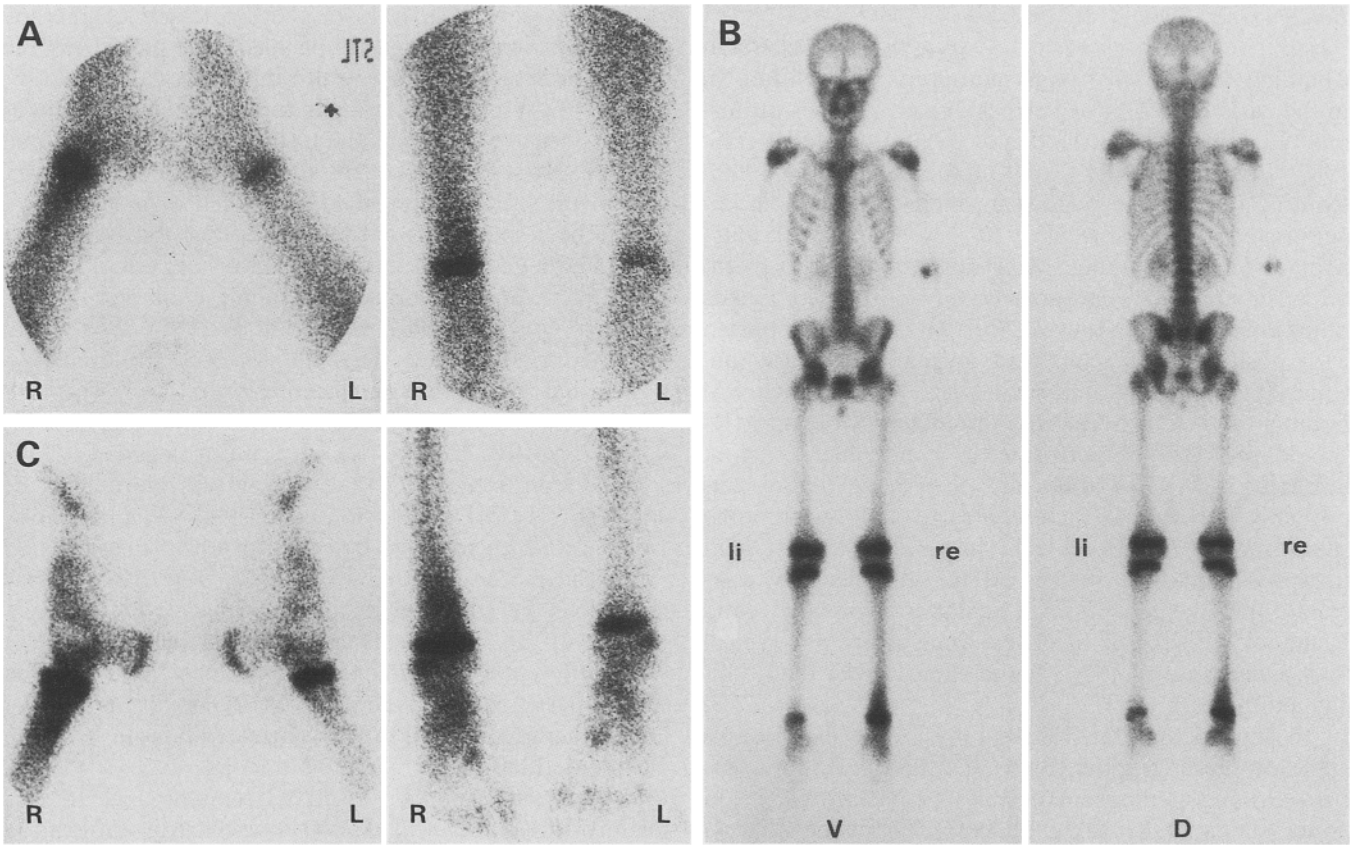

Fig. 11A–C. Bone scan of a 10-year-old girl with osteomyelitis in the right distal tibia. Blood pool images (**A**), whole body scan (**B**) and spot images (**C**)

Child abuse

Recognition of child abuse is the first and decisive step – not only towards adequate therapy – but to prevention as well. X-ray plays a central role in the detection of child abuse, mainly because of the high frequency of skeletal injuries and because most reports of child abuse rely heavily upon radiological findings (Kleinman 1987).

As a screening tool for skeletal lesions, many children's hospitals perform a radiographic survey of the whole skeleton in one projection. Regions of suspected abnormality are radiographed in additional views. After 10 to 14 days, this initial "skeletal status" has to be repeated, because a minimum of 6 to 8 days is required to see periostal calcifications.

A radionuclide bone scan is useful to improve the diagnosis of child abuse and to decrease radiation exposure for those children without skeletal lesions (Tröger 1979; Haase et al. 1980; Smith et al. 1980). The question of whether bone scintigraphy, in cases of suspected child abuse, should be the primary screening modality applied or not is a subject of wide debate (Berdon 1981; Sty and Starchak 1983; Matin 1983; Jaudes 1984). The following examination scheme may be considered as a compromise towards everyday applicability (Tröger 1978).

In cases where the clinical examination does not give any direct or indirect evidence of a skeletal lesion, radionuclide bone scanning should be performed as a first-line investigation. If no abnormalities are detected, X-ray studies are not required, except for the skull, because X-ray is superior in the assessment of skull fractures in children.

In contrast, radiographs of all areas showing abnormal tracer uptake should be performed to provide optimal diagnostic accuracy. This should be followed by a radiographic survey of the whole skeleton in one projection in order to recognize old skeleton lesions (for example, post-fracture deviations of the long bones nonactive on bone scintigraphy).

When the lesions are only visible on scintigraphy, a radiographic control of the suspected skeletal area is performed 10 days later. If the first physical examination already reveals bone injury, the concerned skeletal regions are assessed radiographically. In a second step, bone scintigraphy is performed and is followed by supplementary X-ray images as a function of the scintigraphic findings. It should be underlined that a time interval of at least 2 days is mandatory between the suspected trauma and bone scintigraphy in order to get an abnormal tracer uptake.

Bone necrosis

The high sensitivity of bone scintigraphy is well known in the early detection of Perthes disease in cases of normal radiograph (Sutherland et al. 1980; Cavailloles et al. 1982; Sty et al. 1988; Garty et al. 1989; Feine 1990). Routine three-phase bone scan, including pin-hole images is required (Danigelis 1976). Experience with magnetic resonance imaging (MRI) suggests that this method is superior to scintography; in addition, it avoids radiation exposure. However, certain cases are reported with positive bone scans and normal MRI early on, which have become abnormal later. When the clinical findings suggest femoral head osteochondritis, an MRI should probably be performed – if possible in a first instance. If MRI is abnormal, then bone scanning is probably not necessary. In contrast, bone scintigraphy should be performed if MRI is normal. Similarly, scintigraphy should be performed in other osteonecrosis conditions, e.g. Osgood-Schlatter disease and Kienböck's disease if the X-ray images are not typical (Majd and Frankel 1976; Namey and Daniel 1980; Gilday and Schaub 1985).

In slipped femoral head epiphysis, the diagnosis is made by radiography. Bone scintigraphy shows increased bone metabolism as well as increased perfusion (Smergel et al. 1987; Sty et al. 1988). Following surgery, the bone scan will show closure of the epiphyseal growth plate.

Chronic pain

There is a role for bone scanning in the child with chronic pain (over 2 weeks) when there is a suspicion that the pain may be skeletal in origin. If the radiograph of the affected area is normal, yet the symptoms persist, then a three-phase bone scan is recommended. This clinical situation usually arises in relation to the hip where the differential diagnosis in this non-acute situation lies between synovitis and Perthes disease (Gordon et al. 1987). In the spine, the differential diagnosis includes discitis, a benign bone tumour and excluding the skeleton as a source of the symptoms. It has been suggested that there may be a higher detection rate of spinal abnormalities if SPET were routinely used when the planar images are normal. No formal study has been undertaken to substantiate this hypothesis.

Neuroblastoma

The role of nuclear medicine is to stage the disease at presentation, as well as at various times in the follow-up period. Diagnosis is not usually a problem with these children since the majority of children are ill and present with stage 4 disease. However, since the prognosis remains poor, accurate staging at the end of initial chemotherapy as well as following other stages of therapy would be useful. Great hope has been placed on the potential use of MIBG to fulfil this gap.

^{99m}Tc-MDP bone scan is the accepted method for assessment of skeletal metastasis in neuroblastoma (NBL). It replaced skeletal surveys in the early 1980s. With the introduction of MIBG labelled to ^{123}I, there have been numerous strong suggestions that this agent would adequately assess the skeleton and could replace the ^{99m}Tc-MDP bone scan (Kimmig et al. 1983, 1985, 1986; Feine et al. 1987; Spiegel et al. 1988). Work from Great Ormond Street Hospital for Sick Children suggests that ^{123}I-MIBG may be inferior to the ^{99m}Tc-MDP bone scan in skeletal assessment; no child at diagnosis had a positive ^{123}I-MIBG scan and a negative ^{99m}Tc-MDP scan, suggesting that staging was more accurate using ^{99m}Tc-MDP (Gordon et al. 1990); this has, however, not been reported by other groups. Three isolated cases have been reported where the ^{123}I-MIBG scan was negative, yet the late images of the ^{131}I-MIBG were positive; this may be related to either the dose and/or the different (later) images taken since these children were participating in the ^{131}I-MIBG study as part of their therapy. Detection of the primary tumour has been compared between ^{123}I-MIBG and CT.

The exact role of ^{123}I-mIBG remains unclear; certainly this tracer will detect bone-marrow infiltration while ^{99m}Tc-MDP reflects bone deposits. The apparent insensitivity reported in the literature may be due to this difference. Current staging of NBL is, however, based on skeletal involvement and therefore it is impossible to exclude the ^{99m}Tc-MDP bone scan from the assessment of these children. All imaging techniques, ^{99m}Tc-MDP, MIBG as well as US and CT, have been of little value in determining long-term survival in children who are either in apparent remission at the end of induction chemotherapy or have a good partial response to initial therapy.

Monoclonal antibodies have been used in NBL. In the early 1980s, UJ13A, an Ig A, was used with limited success. Recently, a new murine monoclonal 3F8 (Ig G3 binding specifically to GD2 gangliosode) has been used. Preliminary results comparing this isotope to MIBG are promising (Fletcher et al. 1989).

Lymphoma

Lymphoma, especially non-Hodgkin's lymphoma, is a common malignancy in paediatrics, especially in the very young. ^{67}Ga may be useful in the follow-up of certain children with non-Hodgkin lymphoma. At diagnosis the CT scan offers as much information or more than the ^{67}Ga. However, at follow-up the presence of a mediastinal mass does not imply tumour and therefore CT may overestimate the disease, with one series reporting a false-positive rate of 53% while the ^{67}Ga had a false-positive rate of 5% (Drosman et al. 1990; Anderson

et al. 1983). The phenomenon of thymic rebound is well recognized; neither CT nor ^{67}Ga can distinguish this condition from a pathological increase in size.

Neonatal hypothyroidism

Neonatal screening for congenital hypothyroidism by means of TSH and T4 allows early detection and treatment of affected newborns (Dussault and Laberge 1973; Delange et al. 1977). However, it is still important to differentiate thyroid agenesis from ectopic tissue since the latter might have a slightly better prognosis (Rochiccioli et al. 1989), and neither the initial thyroxine and thyroglobulin levels nor the bone age can definitely establish the diagnosis (Delange et al. 1989).

Echography is the first examination in the presence of an abnormal blood-screening result. This can localize the normal thyroid in all newborns (Chanoine et al. 1990) and thus preclude thyroid dysgenesis (agenesis or ectopic gland). US is challenging and requires a skilled ultrasonographer. Thyroid scintigraphy should be performed only when dysgenesis is suggested by ultrasound and will differentiate between agenesis or ectopic gland (at lingual or hyoid level). A goitre in the neonatal period is not an indication for scintigraphy.

Despite the requirement for a firm morphological diagnosis in the first days of life, treatment for hypothyroidism should never be delayed because the imaging technique (ultrasound and/or scintigraphy) is not immediately available. Scintigraphy can still be performed in the 2 or 3 days following the beginning of treatment with thyroid hormones, because serum TSH remains elevated at least a few days after initiation of therapy.

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