Renal scintiscanning

A review

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Summary

Renal scintiscanning is a simple investigation that does not require special preparation and is well tolerated by patients.

Radiopharmaceuticals used in linear scanning are accumulated in the renal cortex. This accumulation is diminished: (a) when the cortex is destroyed, e.g. by pyelonephritis, injury, etc.; and (b) when the amount available to the cortex is reduced, e.g. by ischaemia. The scintigram depicts the kidneys unimpeded by bowel contents, gives a qualitative assessment of renal function and shows the distribution of zones of normal function. Recent technical improvements show great promise in deriving a quantitative measure of renal function in some circumstances.

The location of normally functioning cortex is often important in the management of renal diseases and the value of scintiscanning is then considerable. It is occasionally useful in planning surgery.

The anatomy of the renal collecting system can be shown only by urography. High dose techniques achieve this even in the face of renal failure, and scintiscanning has few indications in investigating lesions that distort the renal anatomy, e.g. tumours and cysts.

Renal scintiscanning is a very valuable additional method to urography, arteriography and renography in investigation of renal disorders.

Introduction

Scintiscanning is an attractive method of investigation, because it is simple and well tolerated and requires no special patient preparation. The stimulus to increase the use of techniques with such an appeal is so great that it is desirable from time to time to reflect how well they answer the clinical problems, and what place they have achieved alongside more established methods.

During the past decade many uses have been claimed for renal scintiscanning, usually in clinical situations where radiological methods had been the methods of choice (McAfee & Wagner, 1960; Sodee,

1963; Desgrez, Raynand & Kellersohn, 1964; Izenstark *et al.*, 1964; McEwan & Rosenthal, 1966; Winter, 1966; Gottschalk, 1967; Chisholm, Aye & Evans, 1967; Graham *et al.*, 1967). Experience has helped to clarify the indications for renal scintiscanning and the value and application of the results will be discussed in this review.

Details of the physical aspects of scanning can be found elsewhere (Mallard, 1966, 1969) and the available instruments will be mentioned only briefly. The most widely used is the linear scanner in which a detecting crystal collimated to a small area moves continuously to and fro across the area being scanned, taking some 40 min to scan both renal areas. It can be used only with radiopharmaceuticals that are accumulated in the kidneys, because the speed of scanning is relatively so slow. A multiprobe scanner has been designed which improves the speed of scanning considerably (Hayes, Swanson & Taplin, 1968; Hindel, Gilson & Swanson, 1969) but maximum improvement in speed is obtained with the gamma camera, a static detector that can produce an image in a matter of seconds (Gottschalk & Auger, 1965a, b). Lesions are detected as readily as with a linear scanner (McCready, 1967) and because rapid serial images can be produced, compounds that traverse the kidney as well as those that are accumulated can be used. Linear scanning data are recorded on paper by coloured dots, or a radiograph by a photo scan. Gamma camera data are recorded in black and white by Polaroid camera. Evaluation of the data can be enhanced by the use of an image intensifier (Ter-Pogossian, Kastner & Vese, 1963) and digital computer (Tauxe, 1969).

Radiopharmaceuticals

The first compounds chosen for renal scanning were ¹³¹I-labelled pyelographic contrast media, e.g. sodium diatrizoate (Hypaque) but as these are excreted by glomerular filtration they disappear too rapidly from the field of a linear scanner to be usable (Denneberg & Hedenskog, 1959). They were discarded in favour of compounds accumulated in the

kidneys. Typical of these are the mercurial diuretics which are accumulated by the tubule cells and excreted slowly (Borghgraef & Pitts, 1956). The greatest renal accumulation is achieved by 3-chloromercuric-2-methyl propylurea (chlormerodrin) (Kessler, Lozano & Pitts, 1957), which has become the agent of choice.

After intravenous injection, a variable amount of chlormerodrin which is protein-bound is transferred to the tissues, mainly to the kidneys (60%) but also to liver, spleen and muscles. In the kidney, animal studies have shown that all the chlormerodrin is located in the renal cortex, mainly in its inner third, within the cells of the distal convoluted tubule (Laakso, Lindgren & Rekonen, 1965).

Accumulation increases slowly over 1–2 hr and remains steady for about 6 hr before it begins to fall as some of it is excreted in the urine. Ten per cent of accumulated chlormerodrin is retained permanently in the tubule cells (Gottschalk, 1967).

Chlormerodrin can be labelled with either ^{203}Hg or ^{197}Hg , the choice being determined by important biophysical differences between these isotopes (Table 1). The relatively penetrating gamma photons of ^{203}Hg are an advantage in overcoming tissue attenuation in a thick-set patient, but because of its longer half-life and beta emission it gives a much higher renal radiation dose (20–30 rads/100 μCi) than ^{197}Hg (3–4 rads/100 μCi) which is, therefore, generally preferred (Blau & Bender, 1964; Quinn & Maynard, 1965). ^{197}Hg may also be used as a chelate, with ethylenediamine-tetra-acetate which is accumulated in the same way as chlormerodrin (Kraszhai, Pal & Foldes, 1965). Other chelates, e.g. $^{99\text{m}}\text{Tc}$ -iron complex (Harper *et al.*, 1965) have even more favourable physical characteristics (Table 1) and improve the quality of the image without increasing the radiation hazard. Because it produces serial images so quickly the gamma camera can also be used with compounds not accumulated by the kidney, e.g. $^{113\text{m}}\text{In}$ diethylenetriamine-penta-acetic acid, filtered by the glomeruli (Reba, Hosain & Wagner, 1968), or ^{131}I hippuran, filtered by glomeruli and excreted by tubules. The renal radiation hazard is then minimal (Hayes, Swanson & Taplin, 1968). The

serial renal images from these compounds are more akin to the nephrogram and pyelogram phase of excretion urography than to a chlormerodrin image, with the advantage that they are a better test of function than urography (Hayes *et al.*, 1968).

Finally the distribution of renal vasculature can be recorded with the gamma camera and compounds like $^{99\text{m}}\text{Tc}$ which outline the body blood pool, and this can be used in conjunction with conventional chlormerodrin scintigraphy (Rosenthal, 1967).

The choice of radiopharmaceuticals is influenced most by the equipment available, and also by the availability and shelf half-life of the agents. Many will prefer chlormerodrin to $^{99\text{m}}\text{Tc}$ or $^{113\text{m}}\text{In}$ compounds for routine scanning because it can be injected directly from its ampoule without preparation and has an economical shelf half-life.

Technique

The usual dose of ^{197}Hg chlormerodrin for an adult is 100–150 μCi given intravenously. The quantity of diuretic injected is too small to have any detectable pharmacological effect. The patient lies prone so that the scanning head can be brought as close as possible to the kidneys. If an undercouch head is available it is more convenient for the patient to lie supine, and this position is used also when an anterior scan is needed, e.g. in outlining the isthmus of a horse-shoe kidney or a pelvic kidney. The optimal time for scanning is 1–2 hr after injection when the renal accumulation is maximal. A delayed scan may show better accumulation in renal failure. Each scan takes 3–40 min and the whole investigation takes 2–3 hr of the patient's time. The gamma camera produces each image in a matter of seconds and it is as important in saving time as in conducting dynamic studies.

Normal appearances

The scintigram of chlormerodrin and similar compounds shows the distribution of functioning renal cortex, without any contribution from the medulla or collecting system. The count rate is highest over the centre of the image and falls quite quickly towards the margins, which are often unsharp (Fig. 1). The count rate is usually equal over two normal kidneys, but attenuation of activity could occur from the deeper of two kidneys, making the images unequal. The difference in renal depths is probably less than 1 cm (Britton & Brown, 1968) which is probably not significant but a difference of up to 15% maximum count rate has been found between normal kidneys (Morris *et al.*, 1967).

The shape and position of a scintigraphic and a radiographic image correspond well. The length of the scan image is 1 cm or so less, so that renal size

TABLE 1. Physical properties of isotopes used in renal scanning

Compound	Isotope	Emission	Gamma keV	Half-life
Chlormerodrin	^{203}Hg	Beta, gamma	279	47 days
	^{197}Hg	Gamma	77	65 hr
Hippuran	^{131}I	Beta	360	8 days
Neohydrin		Gamma		
Indium-DTPA	$^{113\text{m}}\text{In}$	Gamma	392	1.7 hr
Pertechnetate technetium-iron complex	$^{99\text{m}}\text{Tc}$	Gamma	140	6 hr

FIG. 1. Normal renal scintigram. Note the high slightly asymmetrical central count rate over both kidneys. Their margins are moderately sharp.

cannot be measured accurately from it, but changes in renal size can be followed closely. The scan image can be related accurately to chosen surface landmarks, and can be used as a guide to renal biopsy in both adults (Baum, Rabinowitz & Malloy, 1966) and children (Forland *et al.*, 1967) and to restricting radiotherapy fields (Teffe, 1966).

Abnormal appearances

The scintigram is abnormal only in conditions that affect the renal cortex, either primarily or secondarily. Zones of diminished accumulation create cold areas with low or absent count rate, whereas zones of increased accumulation have a higher count rate. Localized 'hot areas' in a kidney that is otherwise normal are exceptionally rare (see below). The scintigram is unaffected by the uncomplicated lesions of the collecting system, e.g. calyceal diverticula, sponge kidney, etc., which can only be diagnosed by urography (MacEwan & Rosenthal, 1966).

Abnormalities are divided conveniently into four main groups: (a) morphological, (b) renal masses, (c) renovascular disease, and (d) functional.

(a) Morphological

Normal variations in renal outline, e.g. a large upper pole or prominent lateral margin can be confirmed by showing uniform accumulation within the whole renal outline when scintigram and radiogram are superimposed. Congenital abnormalities such as renal ectopia and horse-shoe kidney are often shown best by combining anterior and posterior scans.

Renal ectopia should always be sought in this way if one or both kidneys are apparently absent.

Small and large kidneys are obvious but their causes are not usually predictable from the scan alone. The exception is marked duplex kidney in which there are two distinct renal elements.

(b) Renal masses

Renal masses do not accumulate scanning agents and whether they are carcinoma, sarcoma, cyst or carbuncle they create filling defects in the scintigram as they displace or destroy normal renal cortex. In general the size and clarity of the defect conform with those of the original lesion. Large defects are often ill-defined: (a) because they displace normal cortex away from the scanner so that its activity is attenuated, and (b) in the case of vascular tumours, because the scanning agent is deviated from the normal cortex by the tumour (Figs. 2, 3 and 4).

Functioning tubule cell adenoma is exceptional because it accumulates more chlormerodrin than normal cortex, creating a diagnostic hot area (Caplan *et al.*, 1968). Another diagnostic appearance is that of the multiple defects found in polycystic disease (Fig. 5). They can be recognized before the kidneys are enlarged (Quinn & Maynard, 1965) and even when infusion pyelography has failed because of impaired renal function (Hurwitz & Weigel, 1965).

The radiology of renal masses consists essentially of detecting them and determining their nature. The latter may be clear from the pyelogram, but often devolves on showing whether or not the mass is

FIG. 2. Right renal cell carcinoma. (a) Pyelogram. Right, upper calyces are deformed by a large mass. (b) Scintigram. Right, poor accumulation confined to the lower pole. The margins of the mass are not well-defined.

vascular, as practically all malignant neoplasms are, or avascular, as all cysts are. The scintigram has two important limitations in achieving these aims. Firstly the size and site of the lesions are critical. Lesions at the centre of the renal mass tend to be obscured by normal cortex and even at the periphery 1 cm is the limit of resolution (Quinn & Maynard, 1965). Subcapsular and parapelvic lesions which do not distort the cortex are undetectable. Carcinoma of the renal pelvis is only detected when it invades the cortex, and it is then indistinguishable from a renal cell carcinoma (Morris *et al.*, 1967). Secondly, the vascularity of a lesion can only be assessed when a

gamma camera scintigram using a vascular agent can be compared with a chlormerodrin scintigram showing its site (Rosenthal, 1967). Even then the resolution is far too poor to detect the minimal pathological circulation from which an arteriographic diagnosis can be made.

Pyelography followed by arteriography or cyst-puncture as appropriate remain the methods of choice for investigating renal masses. Scintigraphy is restricted to: (a) contraindications to pyelography, e.g. hypersensitivity to organic iodides; (b) confirming the equivocal pyelogram in which the calyces are normal and the cortex thickened; (c) detecting

FIG. 3. Same case as Fig. 2. Right renal cell carcinoma. Arteriogram. There is a pathological circulation through-out the mass.

multiple cysts, when it is more accurate than pyelography (Morris *et al.*, 1967); and (d) assessing the distribution of normally functioning renal substance, e.g. as a preliminary to therapeutic cyst-puncture in polycystic disease or occasionally before planning surgery for known carcinoma.

(c) Renovascular disease

Accumulation of chlormerodrin by an ischaemic kidney is low because diminished perfusion makes it less available. The size of the image will be small if the kidney is small, and its uptake will be low, and may be irregular. The contralateral renal image is normal except when there are changes due to secondary hypertension, giving it also a mottled pattern (Quinn & Maynard, 1965). Delayed scintigrams taken at 48 hr have been used to estimate the degree of ischaemia more accurately (Schlegel, Varela & Stanton, 1966). The percentage of radio-nuclide then in each kidney is proportional to the percentage of total renal plasma flow, which can be measured readily (Tauxe & Hunt, 1966). A discrepancy between the relative renal plasma flow and the relative radiographic renal sizes is an index of ischaemia needing further investigation (Schlegel,

Merlin & Varela, 1967). Experimental renal artery stenosis is known to cause hypertension (Goldblatt, 1937) and because it is known that in man surgery can sometimes reverse hypertension much interest has been centred on detecting renal artery stenosis. However, not all renal artery stenoses are significant (Sutton, Brunton & Starer, 1961) and the selection of those suitable for surgical treatment requires detailed and painstaking clinical and radiological investigation (Brown, Robertson & Lever, 1968). The final clinical results do not always justify such an exhaustive investigation (Chamberlain & Gleeson, 1965) and simpler screening methods have been sought. Pyelography is of course essential to demonstrate other causes of hypertension (Saxton, 1969). Supported by renography it is a very accurate screening method for ischaemia (Andrews, Parsons & Roebuck, 1965; Luke *et al.*, 1966, 1968). Linear scintigraphy has some use as a screening test (Bellion, Chiarle & Perolino, 1966) but many have found it unreliable (Allen & Riley, 1963; Gyftaki *et al.*, 1966; Graham *et al.*, 1967) because its signs are non-specific and can be misleading. However, dynamic studies with the gamma camera, enhanced by computer analysis have been found much more reliable (zum Winkel, 1968). They have tremendous potential in evaluating the significance of renal artery stenosis, and in selecting patients for arteriography which remains the basis for showing the feasibility of surgery (Sutton, 1968). Showing functional abnormalities in the contralateral kidney is an important function of scintigraphy.

Finally the accuracy of diagnosing renal infarction can be improved by matching scintigram and pyelogram, and showing that the scan-image does not extend to the renal outline at the site of the infarct (Wisoff & Chambers, 1966).

(d) Functional

The distribution and intensity of accumulated agents reflect the location and functioning capacity of the renal cortex. This knowledge is important in the management rather than the diagnosis of conditions discussed in this section. In severe renal failure, renal accumulation of chlormerodrin is reduced and the image becomes ill-defined and mottled. When the blood urea is below 80 mg/100 ml useful scans can be obtained, but the upper pole of the right kidney is often obscured by hepatic uptake (Chisholm *et al.*, 1967). An improved image is claimed by delaying the scan (Baum *et al.*, 1966). The count rate may then be deceptively high in the better of two poorly functioning kidneys (Rosenthal, 1966). As a rule the scintigram is of dubious value when the blood urea is markedly raised (Graham *et al.*, 1967) though it has sometimes been found useful when pyelography

FIG. 4. Multiple cysts left kidney. (a) Scintigram. Right, normal; left, diffusely poor accumulation. Individual cysts cannot be identified. (b) Arteriogram. The nephrogram phase shows several avascular filling defects.

has been unsuccessful (Bellion *et al.*, 1966) and can be a useful alternative in these circumstances. In some cases of renal failure ^{131}I ortho-iodohippurate becomes relatively fixed in the kidney and may give a good scintigram when even the urogram is uninformative (Rosenthal, 1966).

The size of renal stones and their relationship to the calyces can only be shown by a pyelogram but the pyelogram does not show the local impairment of function often associated with multiple stones or staghorn calculi. This information can be derived from a scintigram and can be useful in conserving appropriate renal segments at lithectomy (Fig. 6).

Experimental total ureteric occlusion in the dog shows deterioration of scintigram function within 24 hr, and the degree of recovery that is possible can be judged from the scintigram (Johnston & Murphy, 1966). The implications of this knowledge in managing ureteric calculus are clear but have yet to be exploited.

In managing hydronephrosis it is important to know the severity of pelvi-calyceal obstruction and its associated parenchymal damage. The anatomical disorder can be shown only by urography, but this is an unreliable way of assessing the function of a thin rim of cortex stretched over a large hydronephrotic

FIG. 5. Polycystic disease. The multiple well-defined filling defects are diagnostic.

FIG. 6. Multiple renal calculi. (a) Plain radiogram. (b) Scintigram. Accumulation is least at the sites of the larger calculi.

FIG. 7. Left hydronephrosis. (a) Pyelogram. Left kidney is very faintly outlined. (b) Pre-operative scintigram. Right, normal; left, very poor accumulation. (c) Six months after pyeloplasty. Left, accumulation is already improving.

FIG. 8. Renal tuberculosis. (a) Pyelogram. Right, upper calyces are not visualized. (b) Scintigram. Poor accumulation in right upper pole is more extensive than the urogram suggests.

sac. Scintigraphy give a much better estimate of residual function, though considerable attenuation can occur if the hydronephrotic sac is large enough to displace normal cortex away from the skin surface. Although recovery of function after reconstructive surgery is usually slow when the impairment is severe, it can be quite dramatic (Fig. 7) and claims that absent scan function is a contraindication to reconstructive surgery (Quinn & Maynard, 1965) should be viewed with caution. Scintigraphy is useful in deciding the order of treatment in bilateral hydro-nephrosis.

When partial nephrectomy is being considered for tuberculosis the full extent of the disease must be known as accurately as possible, and a scintigram often shows that the disease is more extensive than the pyelogram suggests (Bollini & Tori, 1964) (Fig. 8).

Several reports describe the value of scanning in managing renal injuries (Freeman, Kay & Meng, 1966; Kasmin, Swanson & Cockett, 1967). In the experimental animal the scintigraphic abnormality is proportional to the severity of the injury, ranging from simple contusion (normal scintigram) to fragmentation (poor uptake and destroyed profile)

(Betti *et al.*, 1966). In man some minor injuries have been shown more readily by scintigraphy than urography (Freeman *et al.*, 1966). Scintigraphy is a reliable way of location of functioning renal cortex, particularly in the uninjured kidney, and as a baseline for following up treatment. The management of renal injuries is usually conservative (Slade, Evans & Roylance, 1961; Roberts & Slade, 1964) and where adequate pyelography is available, supported where necessary by arteriography, scintigraphy offers no essential additional information.

The investigation of renal transplants by radiography and scintigraphy is becoming increasingly important. A transplant that is functioning normally accumulates chlormerodrin well. If anuria or oliguria occurs, rejection can usually be distinguished by standard methods of investigation. If the evidence from these tests is equivocal or suggests rejection, a scintigram can produce useful additional information, because a normal or slightly impaired accumulation has a good prognosis, and is evidence against rejection which usually has no uptake (Figueroa *et al.*, 1965).

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