Abstracts in this section pertain to papers to be presented at the Seventh International Symposium, Radionuclides in Nephro-Urology, May 7-10, 1989, Williamsburg, Virginia. Chairmen: M.D. Blaufox, MD, PhD, N.K. Hollenberg, MD, PhD, C. Raynaud, MD.

^{99m}Tc-MAG$_3$: CHEMISTRY AND BIOKINETICS OF BY-PRODUCTS

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Recently ^{99m}Tc-labelled mercaptoacetyl triglycine (MAG$_3$) has been discussed as a replacement of radioiodinated ortho-iodohippuric acid (OIH) in renal function studies.
One major problem using MAG$_3$ seems to be the biodistribution of by-products which occur during the labelling procedure. Several authors reported about different liver uptake of "Kit-prepared" and "HPLC-purified" ^{99m}Tc-MAG$_3$ respectively. In order to investigate the influence of these impurities on renal function studies, we isolated the by-products from our own kit preparations, evaluated their biodistribution in rats and compared these data with the in vivo behaviour of pure ^{99m}Tc-MAG$_3$ (HPLC-purified, radiochemical yield > 99 %).
Therefore ^{99m}Tc-MAG$_3$ was prepared by stannous cloride reduction of pertechnetate in the presence of its precursor S-Bz-MAG$_3$ and subsequent incubation at 100 °C for 10 min. Typical radiochemical yields were about 94 %. The impurities as well as ^{99m}Tc-MAG$_3$ were isolated by means of HPLC and were investigated in female SD-rats. The scintigraphic studies revealed, that three out of four by-products are eliminated in a high degree by hepatobiliary excretion. The fourth impurity was excreted nearly exculsively by the kidneys, but with a significantly lower rate than ^{99m}Tc-MAG$_3$ itself.
From our clinical results ^{99m}Tc-MAG$_3$ may be a suitable replacement for OIH in renal function studies, provided that a kit formulation is available which delivers the radiopharmaceutical in radiochemical yields greater than 95 %.

HANDLING OF 99M-TC-MAG-3 IN THE KIDNEY

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99m-Tc-mercaptoacetyltriglycine(MAG-3) has recently been introduced as a new radiopharmaceutical for dynamic renal scintigraphy.Its application in clinical investigations makes it important to investigate the mechanism of renal excretion. To measure directly the amount of glomerular filtration micropuncture experiments were performed on superficial glomeruli of rat kidneys.The fluid of Bowman space was collected in 22 glomeruli of 4 rats and analyzed for its content of 99m-Tc-MAG-3[1],125-I-hippurate (OIH)[2] and in 7 glomeruli of 2 rats for 3-H-inulin[2] during constant infusion of these compounds.The ratio to the content in arterial plasma (UF/P) gave the following results: 0.23±0.01 for MAG-3, 0.68±0.03 for OIH, and 1.04±0.04 for inulin.Thus the filtrated amount of MAG-3 is only 23 % of that of inulin. The reason might be a higher binding to plasmaproteins. After completion of the rat experiments the plasma-proteinbinding was therefore measured using centrifugation-millipore-filtration technique (Amicon-centrifree, Massach., USA), showing that 80.0±1.5 % of MAG-3 and 32.2±2.0% of OIH were proteinbound in arterial plasma.Thus in experiments with total renal clearance measurements of MAG-3 or OIH its part of glomerular filtration (proteinfree tracer fraction x GFR) and of tubular secretion (total clearance - filtrated part) can be approximately estimated. From earlier experiments on 7 rats the amount of filtrated and secreted MAG-3 was 0.24 and 2.02 ml/min · g· kidney weigt, respectively. For OIH the corresponding figures were 0.80 and 2.52 , respectively. GFR was 1.18ml/min ·g ·kidney weight.

From these micropuncture and clearance experiments we can conclude that 1) MAG-3 is predominantly excreted by tubular secretion (89% of its renal clearance) 2) the lower renal clearance of MAG-3 is both a result of substantially decreased glomerular filtration (ratio 0.3 to OIH and 0.22 to inulin) and a lower tubular secretion rate (ratio 0.8 to OIH).

1)Kit preparation, Mallinckrodt, Holland 2) Amersham, England

I-131 OIH AND TC-99M MAG3 CLEARANCES MAY NOT BE ACCURATE INDICATORS OF RENAL PLASMA FLOW IN ACUTE RENAL ARTERY STENOSIS OR RENAL ISCHEMIA.

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The clearances of I-131 OIH and Tc-99m MAG3 have been described as indices of renal plasma flow. This assumption is true provided the extraction efficiency remains constant. To test this assumption, we measured the renal extraction of Tc-99m MAG3, I-131 OIH and I-125 iothalamate (Ioth) in rat models of cyclosporin toxicity, ischemia and acute renal artery stenosis by obtaining arterial and renal vein blood samples following 60 minutes of constant radiopharmaceutical infusion. Fisher 344 rats were given cyclosporin-A (50 mg/kg/bid) for 5 days and studied on the sixth day. Renal ischemia was induced in Sprague/Dawley rats by clamping the left renal artery for 30 minutes. A right nephrectomy was performed at the end of the ischemic period and the rats were studied 24 hours later. Acute renal artery stenosis was induced in Sprague/Dawley rats by reducing renal blood flow by approximately 60% using a silk ligature around the renal artery.

	PERCENT OF CONTROL		
MODEL	MAG_3	OIH	Ioth
Cyclosporin Toxicity	89%	88%	88%
24 Hour Post Ischemia	62%	65%	42%
60% Renal Artery Stenosis	68%	62%	27%

The renal extraction of MAG3 and OIH is comparable in all three models but there was a significant decrease ($p<.01$) in the extraction efficiency of the renal ischemia and renal artery stenosis animals compared to controls. For this reason, the plasma clearance of MAG_3 and OIH in these two models may not be an accurate indicator of renal plasma flow.

COMPARISON OF OIH, Tc-99m MAG3 AND IOTHALAMATE IN RENAL ISCHEMIA

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Tc-99m MAG3 is a new Tc-99m renal tubular agent which is expected to replace OIH in many clinical applications. Since ischemic injury is a common problem in renal transplantation, we compared the renal clearance of I-131 OIH, Tc-99m MAG3 and I-125 iothalamate (Ioth) in rats with ischemic injury. The left renal artery was clamped for 30 minutes, released and a right nephrectomy performed. Four groups of animals were studied: a single kidney control group (n=6), and groups studied immediately (n=7), and at 24 (n=6) and 72 hours (n=9) after release of the clamp. The renal clearances (ml/min/100 gm body weight) are listed below:

	Control	Immediate	24hr	72hr
OIH	1.86+0.34	0.57+0.52	1.39+0.22	1.70+0.71
MAG_3	1.42+0.22	0.31+0.28	1.01+0.16	1.41+0.57
Ioth	0.53+0.12	0.11+0.10	0.30+0.07	0.59+0.39

Compared to the control group there was a significant decrease in the renal clearance of all three agents immediately post release and 24 hours after the ischemic period ($p<.05$) but by 72 hours there was no significant difference. The MAG3/OIH and Ioth/OIH ratios were significantly less than controls immediately after the ischemic period but these ratios returned to control values by 24 hours. This study shows that MAG3 performs similarly to OIH in ischemia although MAG3 clearances may be more adversely affected than OIH clearances in severe acute ischemic injury, possibly due to a lower affinity of Tc-99m MAG3 for the tubular transport protein.

Tc-99m MAG3: A ROUTINE RENAL RADIOPHARMACEUTICAL.

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The aim of this study was to test the application of a new tubularly secreted Tc-99m labelled radiopharmaceutical in routine practice and its ability to replace radioiodinated orthohippurate, OIH, and Tc-99m DTPA. First a comparison of simultaneous clearances of 0.5 mCi I-131 OIH and 0.5 mCi Tc-99m MAG3 were made in 12 patients; second, serial studies were performed with 2.5 mCi I-123 OIH and 2.5 mCi Tc-99m MAG3 in 20 patients, and with 10 mCi Tc-99m DTPA and 2.5 mCi Tc-99m MAG3 in 11 patients; and finally 2.5 mCi Tc-99m MAG3 was used routinely in 400 patients: hypertension 41%, outflow disorder 33%, renal transplantation 19% and others 7% with a GE 400A gamma camera linked to a Nodecrest Micas 1000 computer.

Tc-99m MAG3 was prepared by adding standard Technetium generator eluate, diluted with saline to between 3-10 ml, to the MAG3 kit vial (Mallinckrodt). Investigation showed that subsequent to the 10 minute boiling step freezing aliquots of the preparation would enable the maintenance of over 95% purity for over eight hours, with re-thawing just before use. Impurities contribute to the 3% liver uptake which is independent of renal function.

The following results were obtained: Clearance OIH = 1.5 MAG3+40 ml/min (+8% SEM). Similar half life ratio MAG:OIH 1.09:1 but smaller volume of distribution MAG:OIH 0.65:1. Relative functions were highly correlated: MAG3:OIH r=0.97 P 0.001: MAG3:DTPA r=0.94 P 0.001. Parenchymal transit times were well correlated: MAG3:OIH r=0.81 P 0.05; MAG3:DTPA r=0.83 P 0.05. Image quality with MAG3 was equivalent to I-123 OIH and better than DTPA especially in renal transplants. Frusemide diurosis responses were similar. No clinical or biochemical side effects were observed.

In conclusion Tc-99m MAG3 combines the physiological properties of orthohippurate with the availability of Technetium 99m and provides a new reliable radiopharmaceutical for routine renal investigations.

A COMPARATIVE STUDY OF RENAL SCINTIGRAPHY AND CLEARANCE WITH TC-99M-MAG-3 AND 123-I-HIPPURATE IN PATIENTS WITH RENAL DISORDERS

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The aim of this study was to compare kit prepared Tc-99m-mercaptoacetyltriglycine, MAG-3, (Mallinckrodt,Holland) with our routine radiopharmaceutical , I-123-hippurate (123- OIH). 17 patients with different nephrourological disorders or hypertension were first studied with 1mCi 123-OIH and then reinvestigated with 2 mCi MAG-3, 2-8 days later.

Renal MAG-3 gammacamera images were almost identical with those of 123- OIH except for higher ($p<0.01$) liver to background (aorta) ratio, 1.75 vs 1.04, at 20 min p.i. irrespective of kidney function.Kidney to background ratio was the same for both tracers, but urinary peristalsis was more clearly and longer visible in the MAG-3 studies. MAG-3 and 123-OIH renograms showed identical relative kidney uptake function ($r=0.99$). Time to maximum uptake correlated less.Time to fall of halfmaximum renal activity was longer ($p<0.01$) for MAG-3 as compared with 123-OIH.

The plasmaclearances of MAG-3 (multiple samples) were lower, 61-±8%,than those of 123-OIH (44 min sample), but significantly correlated($r=0.87$).The plasmadistribution volume (44 min) was lower for MAG-3, as was the content in blood cells (7% for MAG-3 and 27% for 123-OIH, $p<0.01$). The binding of MAG-3 to plasmaproteins was higher, 90% as compared with 74% for 123-OIH, $p<0.01$. The urinary excretion expressed as percent of given dose 60 min after injection was the same for the two substances.

From these differences we conclude that kit prepared MAG-3 has the potential of replacing 123-OIH in routine renal imaging and relative renal function studies in nephro-urological and hypertensive patients. For accurate estimation of renal plasma flow MAG-3 is, however, less suitable since its clearance is substantially lower than that of 123-OIH.

RENAL IMAGING OF THALLIUM-201 DURING CARDIAC THALLIUM EVALUATION. N. Alazraki, J. Ziffer, J. Galt, W. Fajman. Emory University and Veterans Administration Medical Center, Atlanta, GA.

The purpose of this study was to assess the potential role of renal imaging to detect renal hypoperfusion and renovascular or parenchymal disease in patients undergoing myocardial thallium stress imaging. There is an association between coronary artery disease and peripheral vascular, including renovascular, disease. Thus, we routinely image posteriorly over the kidneys immediately upon completion of the stress thallium heart images and also following the delayed (redistribution) heart images. All thallium renal images were recorded on the computer. Quantitative relative uptake of thallium in the kidneys was obtained with background correction. Visual assessments were also performed and compared with the computer quantitative results.

Of 100 consecutive patients studied, 23 had abnormal renal uptake, including asymmetric or focally decreased regions. All of these patients had hypertension requiring multidrug therapy. Four underwent renal angiography; 3 had renovascular disease and one had ureteral obstruction. Others with abnormal thallium renal scans had cysts, emboli, and renal scans. We conclude that thallium may detect renovascular disease or other renal abnormalities and therefore may be a beneficial addition to the thallium cardiac imaging protocols.

THE PERMEABILITY OF THE HUMAN BLADDER TO WATER ASSESSED USING TRITIATED WATER. A.J.W.Hilson, C.A.Lewis, and S.J.Harland, St. Peter's Hospitals and Institute of Urology, London, England.

The permeability of the human urothelium is generally ignored or considered to be negligible, in spite of work both in dogs[1] and in man[2] showing marked flow of water and solutes (including creatinine) across bladder and ureteric epithelium.

We used the method of Fellows (1972) to confirm the permeability of the bladder to water. In 7 subjects 130-200 ml of a sterile solution containing between 1.4 and 4.5 MBq ^3H_2O in isotonic saline was infused into the bladder using a catheter. After approx.40 mins, the bladder was emptied. Blood samples were taken after the infusion. A "spike" of 1.8 MBq ^3H_2O was then injected intravenously, and blood samples obtained to estimate the volume of distribution. Tritium activity was estimated by liquid scintillation counting.

There was rapid flux of the tritium across bladder epithelium, with absorption of between 8.5% and 24% of the instilled ^3H_2O. Since the volume recovered was usually about 50ml greater than the instilled volume, this was presumably a bi-directional flux. Bladder urine cannot be regarded as identical to "fresh" urine.

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[1]Levinsky,N.G. and Berliner,R.W., Am.J.Physiol. 196, 549-553, 1959.
[2]Fellows, G.J. and Marshall, D.H., Invest. Urol, 9, 339-344, 1972.

RENAL TUBULAR REABSORPTION OF CALCIUM IN PRIMARY HYPERPARATHYROIDISM.
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As a continuation of our recently published study of patients with familial hypocalciuric hypercalcaemia (FHH) we have done a similar study in nine patients with primary hyperparathyroidism (PHPT) and nine age sex and surface matched healthy controls. On the previous evening they had taken 16 mmol of lithium as Li_2CO_3. Fasting urine and plasma samples were analysed for calcium and lithium. The glomerular filtration rate (GFR) was determined from the renal plasma clearance of 51-CrEDTA and measured simultaneously with the renal plasma clearance of lithium and calcium. On the assumption that the reabsorption of calcium in the proximal tubule is isotonic (like for sodium)the following parameters were calculated: Proximal fractional reabsorption (PFR), distal fractional reabsorption of calcium (DFR_{Ca}), proximal absolute reabsorption of calcium related to GFR (PAR_{Ca}/GFR), and distal absolute reabsorption related to GFR (DAR_{Ca}/GFR).

We found no difference in PFR between the two study groups, whereas PAR_{Ca}/GFR as well as DAR_{Ca}/GFR were increased in PHPT. These results differ from those recently found in our FHH subjects, where the increased renal tubular calcium reabsorption seems to take place exclusively in the proximal tubule.

In conclusion, our results therefore suggest distinct differences in renal calcium handling between PHPT and FHH and that simultaneously determination of GFR and renal plasma clearance of lithium may be helpful in the differentiation of these two hypercalcaemic disorders.

POSITION DEPENDENT DISCREPANCIES BETWEEN WHITAKER-TEST AND DIURESIS RENOGRAM FOR ASSESSMENT OF OBSTRUCTIVE UROPATHY - A CASE REPORT
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For the definition of obstructive uropathy the "Whitaker-Test" is considered as a "gold standard". The much less invasive diuresis renogram (DNG) although recognized as a valuable method for the distinction between obstruction and delayed outflux from a wide, atonic pelvis does not always produce the same results. Whitaker-Tests are done in an unphysiological prone position, the DNG either in supine or sitting

positions.We tried to clarify therefore whether discrepancies between Whitaker-Test results and DNG-findings could be attributed to these altered conditions. So far only 10 patients were studied. Whitaker-Tests were performed as described in the literature, DNG's were done on day with 120 MBq/kg body weight of 123 I-Orthohippurate under constant hydration conditions once in the prone position and then in supine or sitting position. Results showed that in 1 case a discrepancy between Whitaker-Test and DNG report was due to the unphysiological prone position during the Whitaker-Test. No obstruction signs were observed in the supine DNG while the Whitaker-Test and DNG in prone position produced evidence for "obstruction". In the other cases Whitaker-Test results and DNG reports were identical, when an appropriate interpretation of DNG curves was done (Zechmann W., Nuclear Med. Comm. 9, 283 - 294, 1988). All these possibilities for error should be considered in the interpretation of Whitaker-Tests and DNG's.

RENAL PARENCHYMAL TRANSIT TIME OF TC-99M-MAG_3 FROM FACTOR ANALYSIS AND FROM ROI SELECTION IN HYDRONEPHROSIS. C.D. Russell, M.V. Yester, E.V. Dubovsky. University of Alabama Hospitals and V.A. Medical Center, Birmingham, AL, USA.

Because of thinned cortex and marked pelvic retention, it is difficult to obtain parenchymal time-activity curves free of crosstalk from the pelvis in hydronephrotic kidneys. Factor analysis, in theory, permits separation of time-activity curves even from spatially overlapping organs. Tc-99m-MAG_3, because of its high renal uptake and good statistics, lends itself to this approach. Here we present preliminary findings in a group of seven normal and six hydronephrotic kidneys that were shown to have no significant obstruction (either by diuretic renography or by lack of disease progression on serial studies). For comparison, parenchymal transit times were calculated both from factor analysis and from a two-pixel-wide cortical region of interest (ROI). The range of parenchymal transit times for the 7 normal kidneys was 1.5-3.1 min calculated from the cortical region of interest, 1.5-2.8 min from the factor curves. For the 6 hydronephrotic (but unobstructed) kidneys the range of transit times from the factor curves was 1.8-2.7 min, so that all values fell within the range of normals. Calculated from the cortical region of interest, however, the transit times for the unobstructed hydronephrotic kidneys were prolonged in five of the six cases. One (2.7 min) was at the high end of the normal range, one was 3.5 min, and the other values were greater than 4.3 min. (Since only 5 min of data were processed, exact values were not obtained above 4.3 min.) ROI selection thus yielded falsely abnormal values in 5 of 6 hydronephrotic kidneys.

These findings suggest that factor analysis separates parenchyma from pelvis better than ROI selection, and furnishes a better estimate of parenchymal transit time.

ABNORMAL RENAL MOBILITY: RADIONUCLIDE FEATURES AND CLINICAL RELEVANCE.
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During an 24 month period, 11 patients attending the urological clinic were diagnosed as having abnormal renal mobility. There were 10 females presented with right sided loin pain and had normal urograms, except for one who had minimal renal pelvic dilatation. The male had no pain, but uographic evidence of bilateral idiopathic hydronephrosis.

In every case, ^{123}I-OIH erect scintiscans suggested a small right kidney with reduced split function (range 27%-41%, mean 33%). In the female with pelvic dilatation, and the male, the curves were obstructed. In the remainder, the curve shapes were normal, but reduced or "miniaturised". Similar appearances were apparant on erect 99mTc-DMSA scans. However, split function calculated by taking the geometric means of anterior and posterior images gave normal split function (range 46%-53%, mean 48%). Supine DMSA images showed a normal right kidney, while oblique erect images demonstrated the right kidney to be prolapsing downwards and forwards, the lower pole moving anteriorly, explaining the discrepancies.

Four patients had only mild pain and did not require surgery. Five patients had nephropexy with relief of their symptoms and normal post operative scans erect and supine. The female with coexisting renal pelvic dilatation had nephropexy, but had persisting signs of obstruction and required further treatment. The male patient had nephropexy and pyeloplasty.

Abnormal renal mobility can give erroneous split function estimates in erect renography, and may cause pain in some cases.

THE USES AND INTERPRETATION OF MODIFIED DIURESIS RENOGRAPHY. S.M.UPSDELL, H.J.Testa, R.S.Lawson, R.N.P.Carroll, E.C.Edwards Depts of Nuclear Medicine and Urology, Manchester Royal Infirmary, Manchester, U.K.

Diuresis renography has been widely used in the investigation of abnormalities of the urinary tract for over ten years, yet equivocal results are still obtained in up to 15% of cases. Furthermore discrepancies occur between renography and other methods of evaluation of dilated upper urinary tracts. Since 1982 we have employed a modified method of diuresis renography in which frusemide is given 15 minutes before the radiopharmaceutical (F-15 renography). This ensures a maximal diuresis during renography and helps to clarify equivocal results.

Previous studies have confirmed a significant increase in urinary flow rates during F-15 renography. We have compared F-15 renography with standard diuresis renography using 123I hippuran in 112 patients. A significant increase in 2 minute uptake ($p<0.001$) and reduction in time to peak was demonstrated in the F-15 method. However, when compared with values obtained in the standard diuresis renogram, relative function estimates were not affected by the pre administration of frusemide ($p=0.001$). Equivocal washout occured in 19 patients using standard diuresis renography. F-15 renography clarified washout in 16 of these cases.

The F-15 renogram curve should have a rapid uptake phase, an early peak and a rapid washout phase. If these characteristics are not demonstrated then further investigation of the urinary tract will be required.

It is now our policy to perform F-15 renography in renographically or clinically equivocal cases.

PROSPECTIVE EVALUATION OF RADIONUCLIDE MONITORING IN RENAL TRANSPLANTATION.
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At our transplantation center renal allografts are monitored by radionuclide examinations (131-I-hippuran-renography and/or 99m-Tc-pertechnetate-angiography) 3 times a week until discharge (or graft removal). Since the beginning of 1988 the nephrologist on duty has prospectively answered a questionnaire concerning the consequence of the finding at the radionuclide study in order to investigate the value of the monitoring. After presentation of the result of the examination it was indicated whether nothing (unchanged circumstances or confirmation of progress), another diagnostic procedure, medical or surgical intervention et c. were performed.

A total of 155 radionuclide studies (median: 9, range 1-14) have been performed in 21 consecutive patients (Nov. 88). In 3 patients the postoperative course was uneventful. In 8 cases (7 patients) the radionuclide examination led solely to intervention (4 cases) and another diagnostic procedure (4 cases). The radionuclide finding was correct in 6 of the 8 cases. In 15 cases (11 patients) the radionuclide examination together with laboratory and/or clinical findings indicated a complication, why another diagnostic procedure was performed. Thereafter intervention was done in 7 of the 15 cases. Effect of rejection therapy could be confirmed by the radionuclide studies in 6 of the 7 episodes. No registered complication remained undetected by the radionuclide studies.

It is concluded that radionuclide monitoring is very valuable in the early stages of renal transplantation.

MEASUREMENTS OF Tc-99m MAG3 UPTAKE IN RENAL TRANSPLANT. H.Y. Oei, S. Surachno, J.M. Wilmink, J.B. van der Schoot. Academic Medical Centre, Amsterdam, The Netherlands.

Serial measurements of radioiodinated hippuran (OIH) is useful for the management of renal transplant patients. The aim of this study was to evaluate whether Tc-99m MAG3 can replace OIH for this purpose.

Data were obtained from 80 consecutive patients (pt). In the first 40 pt renography was performed using 20 MBq I-123 OIH, in the other 40 pt 50 MBq Tc-99m MAG3 was used. All pt received ciclosporin - low dose prednisolone as immunosuppressive therapy. The methods applied were described earlier

(Radionuclides in Nephrology 1982, pp 283 - 288) except two modifications: the acquisition of data in 15-sec frames was used instead of list mode and for the MAG3 study the injected dose was calculated by measuring the activity of a standard dose of approximately 10 MBq with the gamma camera. Clinical diagnosis of acute rejection (AR) and ciclosporin toxicity (CT) were supported by fine needle aspiration cytology.

The initial 10-min uptake of Tc99m MAG3 (MAGUP) (range 11 - 42, mean 25, sd 7) was approximately the half of the initial 10-min uptake of I-123 OIH (OIHUP) (range 29 - 80, mean 54, sd 12). In pt with initial oligo-anuria (OA) the uptake was lower than pt showing immediate diuresis. Pt whose course was not disturbed by AR or CT showed an increase of the uptake in the first 14 days, OIHUP (range 56 - 114, mean 84, sd 13) was significantly higher than MAGUP (range 21 - 61, mean 38, sd 9). As in study using OIH, a decrease of MAGUP was observed during AR as well as CT. It appeared that differentiation of AR from CT was not possible. An alteration from accumulation curve into a blood disappearance curve was observed in pt with initial OA superimposed by CT. After converting into prednisone - azathioprine the renogram showed an accumulation type again within a few days. In our opinion MAG3 is a suitable replacement of OIH for renal transplant study.

WILL Tc-99m-MAG_3 REPLACE I-131-OIH AND Tc-99m-DTPA IN THE FOLLOW-UP OF RENAL TRANSPLANTS? EV Dubovsky, CD Russell, MV Yester, B Thorstad, JP Ryan. The University of Alabama and V.A. Medical Center, Birmingham, AL.

Tc-99m-MAG_3 was tested in 28 patients (18 males, 10 females, ages 18-56) with kidney grafts (9 LRD, 19 cadaveric) using a comprehensive renal function protocol (JNM 12:1115,1975). It comprised ERPF measurements (single sample technique) and excretory index (EI) a parameter of transit of the agent through the graft and collecting system. MAG_3 (5 mCi) and OIH (150 uCi) were used with dual channel technique for imaging and counting. The data acquisition included 120 1-sec perfusion frames followed by eighty 20-sec frames together with pre-void and post-void bladder images. Since MAG_3 and OIH clearances are proportional, ERPF was calculated from MAG_3 values using a constant 0.563 (JNM 29:1931,1988).

The diagnosis was made using dynamic patterns of ERPF and EI changes and clinical data: 13 were normal; 7 had uncomplicated ATN, which resolved without therapy; 3 with AR responded to OKT_3, 1 with Cyclosporin toxicity to dose adjustment. 5 patients with combinations of problems had open biopsy, which confirmed the diagnosis in 4. In one patient with ATN and AR, significant infection was missed. ERPF (R=0.96) and EI (R=0.97) correlated well. The MAG_3 images permitted detection of cortical lesions, bladder defects, small hematomas, and poorly functioning native kidneys not seen on OIH images. The time-activity curves and peak times (R=0.99) were similar. Perfusion curves were different from DTPA curves; fast MAG_3 extraction obscured the peak and abolished descending limb.

Tc-99m-MAG_3 can be substituted for OIH in the quantitative protocol with better image quality and favorable dosimetry. Fast MAG_3 excretion with high concentration in the parenchyma and collecting system improves lesion detection over DTPA, while vascular perfusion curves are different.

DIALYSATE SODIUM CONCENTRATION AND SKELETAL MUSCLE AND SUBCUTANEOUS BLOOD FLOW. N. Hammer, J. Kofoed-Johnsen. Dept. Nephrol. Rigshospitalet, DK-2100 Copenhagen, Denmark.

An increase of the sodium content of the dialysate has been reported to diminish the frequency of hypotensive episodes and muscle pains during hemodialysis. The present study was undertaken to evaluate whether an increased sodium concentration has an effect on the regional blood flow in skeletal muscle and subcutaneous tissues. Relative changes of the blood flow were measured by the [133]-Xenon wash-out technique. The activities in two .1 ml depots in cutaneous tissue and muscle tissue in the anterior crural regions were measured by two cadmium telluride detectors fixed to the skin. Ten patients on chronic hemodialysis treatment were studied during two separate regular dialysis treatments with acetate buffered dialysate. The first with a constant sodium concentration (137 mM), and the second with a sodium concentration varying from 147 mM during the first two hours, to 140 mM during the third, and 137 mM during the fourth hour.

Predialysis values of body weights, blood pressures, degree of uremia, and reductions of body weights were equal at the two occasions. Mean BP decreased during the first two hours of HD 12 ± 12 and 18 ± 7 mmHg, respectively. After the first two hours of HD with constant dialysate sodium, the muscle, and subcutaneous blood flow had decreased to 62 ± 12 and 42 ± 16 per cent below basal values, respectively. During the first two hours of HD with high dialysate sodium, muscle and cutaneous blood flow decreased 43 ± 12 and 30 ± 15 per cent, respectively. The calculated vascular resistance in skeletal muscle and subcutaneous tissues increased 400 ± 192 and 135 ± 52 per cent with constant sodium, and only 127 ± 50 and 100 ± 54 per cent with high dialysate sodium, respectively ($p<.05$). There were no differences of the the frequency of hypotensive episodes. However, in those patients who experienced muscle pains, symptoms were clearly correlated to a decrease of skeletal muscle blood flow.

Long term follow up of separate glomerular filtration rate in partially obstructed kidneys.
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In the management of pelviureteric junction stenosis (PUJ), 2 assumptions are regularly found. The first one is that non-operated PUJ will progressively lead to the destruction of the kidney. However, this assumption relies essentially on the observations of total obstruction. The second one is that surgical relief of the obstruction will improve the renal function. This is true for the drainage function, whereas the parenchymal function will improve in a percentage of cases which is variable from one author to the another.

An experimental study was undertaken in order to evaluate on a long term basis the progression of the 99m-Tc DTPA separate glomerular filtration rate (SGFR) in a series of 20 young rats submitted to a partial obstruction of the left ureter. We observed an initial variable postoperative SGFR decrease, depending on the degree of obstruction. However, after this initial period, SGFR remained stable until the natural death of the animal.

The second study was a clinical prospective study on 14 asymptomatic neonates with unilateral PUJ obstruction detected on prenatal ultrasound. When SGFR was abnormal, the patients underwent a pyeloplasty, with the hope to improve the renal function. When SGFR was normal, a conservative attitude was chosen, no matter the other radionuclide parameters (furosemide test or cortical transit). In the operated patients, despite a slight SGFR increase, probably related to the normal renal maturation during the first year of life, SGFR generally remained below the normal range. In the non-operated hydronephrotic kidneys, SGFR constantly remained in the normal range, during a follow up period of 1 to 6 years. In only one patient, we observed a significant SGFR decrease after one year and the patient was shifted into the surgical group. This patient was precisely the only one with a persistent non response to furosemide. It was therefore decided to modify slightly the protocol and to operate the patients with a persistent absence of response to furosemide after the age of 6 months. This protocol should be constantly modulated by the appearance of clinical symptoms or by a sudden increase of hydronephrosis on ultrasound.

SERIAL FUROSEMIDE RENOGRAPHY IN ASYMPTOMATIC HYDRONEPHROSIS DIAGNOSED BY ULTRASOUND IN UTERO AND NEONATALLY. HS Clarke, MM DeBeukelaer, KA Kropp, RR Lenke, WH Persutte, WJ Potvin, Medical College of Ohio, Toledo, OH, USA

Infants referred for evaluation of asymptomatic hydronephrosis (n=17), were serially evaluated using ^{131}I-Hippuran renography with (FR) and without (R) furosemide stimulation. Nine were diagnosed in utero, eight neonatally (Age <4 wks). The renograms were evaluated in conjunction with reflux evaluation, serial ultrasound (US), clinical and laboratory evaluation. The studies were carried out over a seven year period (m=24 months). The renograms were performed a maximum of five times per infant (m=3). The protocol included IV hydration, bladder catheter and sedation. The FR were performed using 1 mg/kg IV, given immediately after the peak activity was achieved. Initial studies without response were repeated with a 2 mg/kg dose. The ^{131}I-Hippuran dose was 0.74 MBq. The infants were classified as nonobstructed (group I) or obstructed (group II) based on FR.

Results: All patients had abnormal R initially. Group I (n=11) had FR with peak activity that returned to baseline with a T 1/2 of 8 minutes or less, post diuretic. Two improved sufficiently on subsequent R to no longer require FR. US in this group demonstrated persistent hydronephrosis in eight, and improvement in two. Group II (n=6), demonstrated FR with a peak activity that remained elevated on a minimum of two sequential studies. All were referred for surgical repair based on these findings. One had repair of an obstructed bladder neck. Three underwent unilateral dismembered pyeloplasty for ureteropelvic junction obstruction. Two are scheduled for repair. Post operative R remained abnormal, but all FR normalized. Pre- and post-operative US showed persistent hydronephrosis. Neither group showed a deterioration in global renal function.

Conclusions: 1) Serial R and FR helps detect mild or improving obstructive hydronephrosis that may not require surgical intervention, 2) serial FR showing no improvement facilitates the decision for surgical repair.

CONSERVATIVE MANAGEMENT OF ANTENATALY DIAGNOSED PELVIURETERIC JUNCTION OBSTRUCTION.

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Eighty children underwent a Tc 99m DTPA scan with diuretic stimulus at 1, 3, 6, 12, 24 and 48 months of age who had an antenatal diagnosis of pelviureteric junction obstruction.

Kidneys with less than 20% function at one month of age had a pigtail nephrostomy and a repeat DTPA scan 3-6 weeks later. Four of these kidneys underwent nephrectomy whilst four showed significant improvement of function and underwent pyeloplasty. Kidneys with differential function of between 20-40% on the three month study, all failed to drain after lasix. Of these 24 kidneys, 4 were not operated on and 3 showed marked improvement of function. The other 20 kidneys underwent pyeloplasty, 10 showed no change in function, 5 showed improved function and 5 had improved to such an exten that function was equal between the two kidneys.

There were 70 kidneys with function greater than 40%. The lasix reponse was variable in this group. Seven of these kidneys showed loss of function on the DTPA scan and underwent pyeloplasty, six of the seven improved to the same function as pre-pyeloplasty, one only improved slightly. Nine children underwent pyeloplasty for urinary tract infection. The remaining 54 kidneys maintain good function with a variable response to lasix.

Kidneys with a differential function greater than 40% may be treated conservatively with close follow up.

DMSA STUDIES IN INFANTS UNDER ONE YEAR OF AGE.

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63 infants under one year of age underwent DMSA renal studies. The indications for this investigation included a grade III or higher vesicoureteric reflux and/or urinary tract infection, with high or persistent fever or severe systemic upset. The DMSA studies were comprised of planar and pinhole views, with some patients also having tomography. These were compared with the clinical history, intravenous pyelography (IVP) and micturating cystograms.

Of the 63 patients, 49 had presented with urinary tract infection (UTI) and 14 had undergone urological investigation for other reasons. In the 49 patients with a history of UTI, 26 had renal cortical abnormalities detected on the DMSA study and 6 had changes of reflux nephropathy on IVP. All infants with abnormal IVP findings had corresponding abnormalities on the DMSA study. Of the other 14 infants, 4 had abnormal DMSA scans and none had IVP changes of reflux.

There was an increasing tendency for DMSA abnormality with increasing grade of reflux. In the UTI group, there was no apparent difference in the incidence of DMSA abnormality between those infants presenting with fever (21/58 kidneys abnormal) and those without fever (12/40 kidneys abnormal). In addition, our results suggested an association between early occurence of UTI and increased rate of scarring.

We conclude that 1. It seems likely that DMSA scanning is more sensitive than IVP in the early detection of renal scarring in infants; 2. There is no relationship between the severity of symptoms in an infant with UTI and the risk of renal scarring; 3. The presence of abnormal scans in some children without UTI suggests that renal scarring may occur with sterile VUR.

PARADOXICAL INCREASED GLUCOHEPTONATE UPTAKE IN EXPERIMENTAL RENOVASCULAR HYPERTENSION.

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99m-Tc glucoheptonate (Tc GHA) accumulation was studied in an experimental model of renovascular hypertension (two kidneys,one renal artery clamped). Two groups of rats were evaluated based on the function of the clamped kidney CIK): I) mild function reduction (ERPF >0.6 ml/min/100g Bwt), and 2) severe function reduction (ERPF <0.6 ml/min/100g). Tc GHA uptake per g of kidney was measured with captopril administration (1.7 mg/100g Bwt) and without captopril administration. ERPF was measured pre and, in animals receiving captopril, post captopril. 50 uCi (0.1 ml) Tc GHA was injected following the ERPF study. The kidneys were removed 3-5 min after Tc GHA administration. After captopril the rats (n=11) with CIK ERPF >0.6, had a higher Tc GHA uptake (6.9%±0.5 S.E.) in the CIK than in the normal kidney (NK) (4.9%±0.2, p <0.003). The rats (n=7) with initial CIK ERPF <0.6 had a lower Tc GHA uptake in the CIK (1.5%±0.3) than in the NK (4.5%±0.9, p <0.002). Tc GHA uptake between >0.6 ml/min/100g and <0.6 ml/min/100g groups after captopril treatment was significantly different in the CIK (p <0.005). In the NK the Tc GHA uptake was not significantly different. Tc GHA uptake between no captopril and captopril treated groups was significantly different both in the CIK (p <0.0025) and NK (p <0.0005) when the initial ERPF was >0.6. In the animals with mildly impaired renal function (>0.6 ml/min/100g), the Tc GHA uptake increased paradoxically after captopril treatment. With severely depressed renal function (<0.6 ml/min/100g) Tc GHA uptake decreased as was expected.

CAPTOPRIL-STIMULATED RENOGRAPHY VS RENAL VEIN RENINS (RVR's) IN TWO-KIDNEY, TWO-CLIP (2K,2C) HYPERTENSION.

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As bilateral atherosclerotic renal artery stenosis is being more frequently recognized in our aging population, debate exists over the renin-dependency of individual kidney function and the concomitant hypertension. Previous studies from our laboratory suggested that captopril (C) lowered mean arterial pressure (MAP), reduced kidney function and altered the renogram of the stenotic kidney in a 2K,1C model (renin-dependent), yet failed to significantly alter kidney function or the renogram in a 1K,1C (volume dependent) model (J Nucl Med 28:1171, 1987). We examined the effect of C upon MAP, C_{IN}, C_{PAH}, RVR's and renography with Tc-99-DTPA and I-131-Hippuran of each kidney in a canine model of 2K,2C hypertension (n=9).

Following the creation of bilateral stenosis (40-60% and 50-80% reduction), the elevation of MAP was significantly lowered (148±7 vs 119±10 mmHg, p<.002) after C (1.5 mg/kg bolus and 1.5 mg/min infusion). C also reduced total GFR (p<.005) with reductions in both the more stenotic (MS) kidney (13.9±4.1 vs 5.4±2.2 ml/min, p=.01) and less stenotic (LS) (24.6±3.8 vs 18.6±3.1 ml/min, p<.06). Baseline and stimulated RVR's correlated inversely with ipsilateral C_{IN}, C_{PAH}, Hippuran uptake and cross-sectional area of the arterial lumen. C enhanced the RVR ratio (MS/LS) from 3.4 to 4.7 and similarly enhanced the diagnostic sensitivity of the time-activity curves for both the Tc-DTPA and I-131 Hippuran renograms in all dogs studied. The changes in Tc-DTPA uptake of each kidney after C correlated with the reductions in C_{IN} (<.005).

Captopril renography may be a suitable noninvasive tool to complement, or supplant, invasive RVR's as an index of renal perfusion and function in 2K,2C hypertension.

PARAMETRIC IMAGING OF RENAL FUNCTION IN RENOVASCULAR HYPERTENSION

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The parametric imaging that we have developed reduces the acquired scintigraphic data into a small number of digital images. Each parametric image displays a specific renal function. The purpose of this study was to determine the usefulness of parametric imaging in patients with renovascular hypertension. Fifty-five patients with arterial hypertension (42 renovascular and 13 essential hypertension) had renal scans with mercaptoacetyltriglycine (MAG_3). Parametric images of perfusion, tubular extraction and mean transit times were calculated by deconvolution analysis of pixel-by-pixel time-activity curves. In 36 patients peripheral and renal vein renin activities were determined. In 21 patients, parametric images were obtained before and after Captopril challange.

In patients with hemodynamically significant renal artery stenosis ERPF and extraction were decreased and the parenchymal transit time was prolonged. These parameters further deteriorated with Captopril challenge. In patients with unilateral stenosis who had improvement of hypertension following reconstructive surgery of the renal artery, ERPF increased and the parenchymal transit time became shortened.

With MAG_3 high quality parametric images can be obtained due to high count statistics. These parametric images may improve accuracy in diagnosing a hemodynamically significant

renal artery stenosis and they allow a quantitative follow-up of renal function following reconstructive renovascular surgery.

DETECTION OF RENAL ARTERIAL STENOSIS BY MEANS OF CAPTOPRIL RENOGRAPHY WITH Tc-99m DTPA.
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To evaluate the diagnostic capabilities of renal scintigraphy after angiotensin-converting enzyme inhibition in detecting renal artery stenosis (RAS), 105 patients, referred for hypertension, were submitted to conventional renal scintigraphy followed 1 to 2 days later by a second study performed after premedication with 50 mgr of Captopril. Renal angiography, by arterial catheterization in all cases, was carried out within 30 days. 55 patients had no RAS, 29 had unilateral disease and 21 bilateral. RAS significativity was set at 50% arterial lumen reduction.

68 patients (Group 1) were considered negative (no RAS or RAS <50%), 25 had unilateral RAS >50% (Group 2) and 12 had RAS bilaterally >50% (Group 3).

Of the first group significant RAS was ruled out in 66/68 cases. Moreover 13 patients affected by nephropathies other than RAS were correctly diagnosed as having no main renal artery stenosis by means of the provocative test, while their baseline studies proved to be falsely positive. In the second group, Captopril administration identified 23/25 patients with unilateral RAS >50%. In bilateral RAS >50% the test proved to be positive in 11/12 patients.

Two patterns of positive response were identified: marked decrease of tracer uptake from the affected kidney (often though not always present in unilateral RAS) and marked delay of tracer appearance into the pelvicalyceal system (typical of bilateral disease and frequent in older patients with unilateral RAS).

Evaluation of parenchymal transit time by deconvolution analysis demonstrated a significant decrease of PTT in normal kidneys ($p<.05$) while stenotic kidneys showed a significant increase ($p<.05$); changes in kidneys affected by nephropathies other than RAS were barely significant ($p=.05$). After Captopril administration PTT behaves very differently in normal as opposed to stenotic kidneys ($p<.001$), .

Overall, Captopril renography had a sensitivity of 92% and a specificity of 98%.

Thus renal scintigraphy after angiotensin-converting enzyme inhibition is suggested as the first test to be performed in hypertensive patients referred for renal scintigraphy. If the test turns out negative, hypertension sustained by RAS can be reasonably ruled out. Only in the case of equivocal results is a second study required in baseline conditions to accurately diagnose the presence of a RAS >50%.

THE MEASUREMENT OF INTRARENAL PLASMA FLOW DISTRIBUTION, IRPF, IN ESSENTIAL HYPERTENSION - THE EFFECT OF ANGIOTENSIN CONVERTING ENZYME, ACE, INHIBITION.
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The aim of the study was to investigate the effect of a new ACE inhibitor, Ramipril, on IRPF in a placebo controlled crossover study in essential hypertension, EH, using the I-123 orthoiodohippurate, OIH, transit time method, previously validated in man and by microspheres in animal experiments. Long loop juxtamedullary nephrons, JMN, have a longer mean transit time than short looped cortical nephrons, CN. This bimodal distribution is obtained by deconvolution analysis of an input function from the left ventricle and the activity time curves obtained from the parenchyme (mix of CN and JMN) and from an outer cortical region (mainly CN) using a cross correlation technique for noise reduction. Comparison of the heights of the CN and JMN transit time distribution curves gives the proportions of plasma flow to each population.

7 EH patients were studied twice using a computer linked GE 400A gamma camera, either on placebo or Ramipril 10mg each for two to four weeks. Cardiac index, CI, total effective renal plasma flow, ERPF, relative renal function and IRPF were determined after a 2.5 mCi intravenous injection of I-123 OIH or a 2.5 mCi injection of Tc-99m mercaptoacetyl triglycine, MAG3. 'ERPF' from MAG3 was corrected by: OIH clearance=1.5 MAG3 clearance + 40ml/min. Results were corrected to the placebo cardiac index to obviate the effects of differing cardiac outputs on ERPF.

Comparing placebo and Ramipril, systolic and diastolic BP were reduced from 172 + 6 to 148 + 10 and 107 + 5 to 90 + 5 respectively $P<0.05$. Changes in CI and ERPF were not significant although ERPF rose from 483 + 20 to 564 + 60 ml/min. CN flow increased from 207 + 7 to 257 + 21 ml/min ($P<0.05$) while CN% of IRPF increased from 85 + 2% to 91 + 2% ($P=0.05$).

In conclusion as previously with Captopril, we have shown a significant increase in cortical nephron flow without a significant increase in ERPF indicating correction of an angiotensin dependent reduction in cortical nephron flow in these patients with essential hypertension, which may be relevant to the aetiology and to the long term management of this disorder.

RENAL VEIN RENIN vs PERIPHERAL PLASMA RENIN COMBINED WITH GAMMA CAMERA RENOGRAPHY IN DETECTION OF RENOVASCULAR HYPERTENSION
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Measurement of renal vein renin (RVR) is an instrument to decide if a renal artery stenosis (RAS) is hemodynamically significant or not. Another method to evaluate the significance of RAS is gamma camera renography (GCR) before and after ACE-inhibition. The purpose of this study is to evaluate whether the combination of peripheral plasma renin with GCR could replace measurement of RVR thereby omitting bilateral renal vein catheterization.

The material consisted of 27 patients with hypertension and RAS on one or both sides shown by renal arteriography. Bilateral renal vein catheterization was performed after 3-4 days with low sodium diet and modified medical treatment in order to increase sensitivity of the renin-angiotensin system. Blood samples were taken from the radial or brachial artery and both renal veins simultaneously before 5 min and 30 min after the injection of 1.25 mg enalaprilate i.v. GCR with 99Tc-DTPA was performed before and 3 h after the injection of enalaprilate. The results are summarized in the following table.

		GCR positive	GCR negative
Lateralization of RVR	Yes	13	6
	No	0	8

Our results indicate that GCR before and after ACE-inhibition corresponds to RVR measurements in 2/3 of patients investigated for renovascular hypertension. Therefore, in 1/3 of patients with renovascular hypertension who have significant increase in peripheral renin by stimulation with ACE-inhibition but no lateralization on GCR, renal vein catheterization is the only method to decide whether a RAS is hemodynamically significant.

CAPTOPRIL RENOGRAPHY (CR) AND DUPLEXSONOGRAPHY (DS): COMPARISON OF TWO NONINVASIVE METHODS FOR THE DIAGNOSIS AND FOLLOW UP IN RENOVASCULAR HYPERTENSION (RVH).
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CR and DS was performed before and after percutaneous transluminal angioplasty (PTA) in 12 pat. with renal artery stenosis (RAS) and hypertension.
Renography with I123 oIH and Tc99m DTPA was done without and with Captopril (25 mg). Diagnostic criteria for RVH: delay in peak activity I123 oIH captopril renogram > 2 minutes compared to baseline renogram and/or decrease of Tc 99m DTPA uptake > 20 % for the captopril study in comparison with the baseline renogram.
For Duplexsonography (realtime sector scanner - 3.5 to 5 MHz - combined with as 3 MHz pulsed Doppler) a systolic frequency shift of more than 5.5 kHz together with spectral broadening was considered as specific for RAS.
In 4 pat. due to individual anatomical conditions DS was not interpretable. 6 pat. had pos. CR and pos. DS; after PTA CR was neg. in all, DS remained pos. in one pat. of this group despite a blood pressure normalization and a normal angiographic result after PTA. In one pat. CR was pos. and DS neg., the hemodynamic relevance of the RAS in this pat. (degree of RAS 60 %) was confirmed by the blood pressure improvement after PTA. In one pat. both studies were neg. before PTA (degree of RAS < 50 %) and no blood pressure change was obtained after PTA. In one pat. with a control CR and renin values suggestive for restenosis, DS was correctly neg. as confirmed by angiography.
DS showed a high rate of non interpretable results and is in contrast to CR operator dependant. However since DS assesses mainly the morphological conditions in RAS and has no concomitant radiation burden, its supplementary use to CR may be justified.

ALTERATIONS OF 131-I METAIODOBENZYLGUANIDINE BIODISTRIBUTION IN IMPAIRED RENAL FUNCTION **L. M. Fig, B.Shapiro, M.C. Tobes, O. Geatti, J.C. Sisson, J. Carey. Division of Nuclear Medicine, University of Michigan Medical Center, Ann Arbor, MI**

131-I Metaiodobenzylguanidine (MIBG) is efficacious in scintigraphic portrayal of pheochromocytomas of all types. MIBG is excreted primarily unmetabolized through the urinary tract. Thus, impaired renal function would be expected to alter its biodistribution and kinetics. We compared the MIBG scintigraphy and blood clearance kinetics in an anephric patient on hemodialysis, two patients with renal insufficiency (serum creatinines 3.7 and 2.4mg/dl) and four patients with normal renal function. Hypothesis : biodistribution of MIBG is altered in anephric and renal insufficiency patients. Findings: 1) Scintigraphy: in the anephric patient background activity was higher and adrenal uptake more prominent than in patients with normal renal function. This probably resulted from sustained, high blood radioactivity and thus presentation of more tracer to the tissues. No bladder activity was seen. In renal insufficiency count rates were higher than normal and inversely proportional to creatinine clearance. 2) Clearance of MIBG activity from the blood of the anephric patient was unusual, in that after an initial fall there was a secondary rise. There was no or only slight decrement of blood activity following 2 hemodialyses. In patients with renal insufficiency the total blood radioactivity fell more slowly than in patients with normal renal function (time to half activity renal insufficiency 9.9 min vs normal renal function 6.9 min.)

3) Distribution of radioactivity between plasma and red cell fractions in renal failure was unusual in that a higher than normal fraction of activity was present in the plasma. Porcent radioactivity in plasma correlated significantly with serum creatinine. (anephric 89% vs. controls 15%). 4) As a result of abnormal clearance, radiation dosimetry is altered in renal disease. In the anephric patient the absorbed radiation dose to blood was 2170 mrem, 190 mrem in a patient with renal insufficiency and averaged 70±20 mrem in patients with normal renal function.

Conclusions: In the face of renal insufficiency alteration of the biodistribution o MIBG must be taken into account in scan interpretation; altered clearance and kinetics affects dosimetry so that dose adjustments may be necessary for scanning or for internal radiotherapy for pheochromocytoma.

COMPARISON OF STANDARD FUROSEMIDE METHOD WITH DIRECT INTRAPELVIC INFUSION IN DIURETIC RENOGRAPHY. K Itoh, K Taniguchi, M Nantani, K Nonomura, M Furudate and T Koyanagi. Department of Nuclear Medicine and Urology, Hokkaido University, Sapporo, Japan.

In diuretic renal scan, completely obstructed excretion pattern was occasionally observed in patients with patent urinary system. In 15 patients with nephrostomy due to hydronephrosis, urinary drainage patterns were compared by two different methods. Standard furosemide renography (indirect diuresis, IDR) was done as follows: 300 ml of water was given orally 20 min. before the scan, then non-diuretic renography was recorded for 20 min. after the i.v. injection of Tc-99m-DTPA to the supine patient, and thereafter the post-voiding diuretic data were collected for 15 min. with the i.v. injection of furosemide (0.4mg/Kg, maximum=20mg). The intrapelvic infusion (direct diuresis, DR) was performed in the same patient as follows: 1mCi of Tc-99m-DTPA was administered into the renal pelvis through a tube of nephrostomy and thereafter normal saline was infused at speed of 3 drops per sec. Diuresis was categorized into four groups according to a half clearance time(DT1/2) of time-activity curve of the whole renal pelvis. It was considered normal (I) when DT1/2 is less than 10 min., undetermined (II) between 10-20min., stenotic (III) over 20 min. and obstructed (IV) increased with time. Three patients of grade IV in IDR was found not obstructed by DR, as were two of grade III and one of grade II. Regression of DT1/2 between IDR (X) and DR (Y) in non-obstructed groups of IDR was $Y=1.44 + .017X$ ($r=0.651$, $p<0.05$). No relationship between split renal function and DT1/2 of IDR was observed.

Diuretic renography seems to be greatly affected by applied manner of diuresis, particularly in large capacity of dilated urinary system.

Abstracts

Abstracts in this section pertain to papers presented at the Spring Meeting of SNM's Central Chapter, "Quantitative Nuclear Medicine," March 9–11, 1989, Chicago, IL.

MORPHINE AUGMENTED CHOLESCINTIGRAPHY: ITS EFFICACY IN DETECTING ACUTE CHOLECYSTITIS. H. Balon, D. Fink-Bennett, T. Robbins, D. Tsai. William Beaumont Hospital, Royal Oak, Michigan.

Cholescintigrams were performed in 158 patients suspected of acute cholecystitis following a 2-4 hour fast and the I.V. administration of 5 mCi of Tc-99m mebrofenin. Anterior images of the hepatobiliary tree were obtained at 10 minute intervals X 6. Morphine sulfate (0.04 mg/kg) was given I.V. if there was non-visualization of the gallbladder at 40-60 minutes provided radiotracer was seen within the small bowel. Acute cholecystitis was deemed present if there was non-visualization of the gallbladder 30 minutes post morphine administration. No cystic duct obstruction was present if the gallbladder visualized within 40 minutes of mebrofenin administration or following morphine.

The final diagnosis (Dx) was established in 51 post-op patients histologically, the remainder having the final diagnosis gleaned from their medical records. 5/158 patients who had an indeterminate cholescintigram (persistent non-visualization of the biliary tree and small bowel) were excluded from analysis. The results are as follows:

	Number of Patients	True + Path Dx	True + Med Dx	True - Path Dx	True - Med Dx	False + Path Dx	False + Med Dx	False - Path Dx	False - Med Dx
Augmented:	61	30	5	4	19	1	0	2	0
Non-Augmented:	92	0	0	14	78	0	0	0	0

The sensitivity, specificity, positive and negative predictive value of morphine augmented cholescintigraphy in detecting acute cholecystitis are 94.6, 99.1, 97.2, and 98.3%, respectively. These findings indicate that morphine augmented cholescintigraphy detects acute cholecystitis with as high a degree of accuracy as routine hepatobiliary scintigraphy yet requires only 1.5 hours to establish the diagnosis.

CORRELATION OF Cu(PTSM) LOCALIZATION WITH REGIONAL BLOOD FLOW IN THE HEART AND KIDNEY

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PURPOSE

The widespread application of positron emission tomography (PET) in clinical nuclear medicine has been hampered by the expense associated with operation of an in-house cyclotron for radionuclide production. We are, therefore, interested in the identification of compounds that can be labeled with generator-produced positron-emitting nuclides and provide clinically useful diagnostic information. In animal model systems we have shown that copper-labeled copper(II) pyruvaldehyde *bis*(*N*-methylthiosemicarbazone), Cu(PTSM), affords relatively high concentrations of activity in the heart and kidneys upon intravenous injection, followed by prolonged microsphere-like retention of tissue radiocopper (Green, *et al., J. Nucl. Med.* 29:1549-1557; 1988). When labeled with generator-produced copper-62 ($t_{1/2}$ = 10 minutes) this compound might serve as a PET radiopharmaceutical for evaluation of regional myocardial and renal perfusion. To better evaluate this possibility, we have examined the correlation between relative regional radiocopper uptake and [Sr-85]-microsphere blood flow in a dog model of myocardial ischemia.

METHODS

In four pentobarbital-anesthetized dogs the left anterior descending coronary artery was ligated to create a zone of ischemia. Five to ten minutes following ligation, [Cu-67]-labeled Cu(PTSM) was administered intravenously. After an additional 2-3 minute delay, [Sr-85]-microspheres were injected into the left ventricle via a catheter inserted through a femoral artery. Arterial blood samples were drawn at a constant rate for one minute following both the Cu-67 and Sr-85 injections. The animals were sacrificed ca 3 minutes post-[Sr-85]-injection and the heart and kidneys excised and dissected for counting to determine regional Sr-85 and Cu-67 concentrations. Relative regional copper-67 levels and relative regional microsphere blood flow were each calculated as the ratio:

$$\frac{(\text{cpm} \cdot \text{g}^{-1})_{\text{tissue sample}}}{(\text{cpm} \cdot \text{g}^{-1})_{\text{reference region}}}$$

for both the heart and kidneys, using the high-flow tissue sample of that organ as the reference region. Absolute microsphere blood flow (ml/(min · gram)) was also calculated for each tissue sample.

RESULTS

The dog model of myocardial ischemia employed in this study afforded an excellent gradient in regional myocardial perfusion; the samples of myocardium most affected by LAD ligation generally had flow reduced by over 90% relative to normally perfused reference regions. In all the dogs studied, an excellent linear correlation was obtained between relative regional radiocopper concentration and relative regional perfusion. Figure 1 illustrates this relationship for a typical dog. Similar results were obtained for each of the three remaining animals.

In the kidney as in the heart, for each animal an excellent linear correlation was observed between relative regional radiocopper concentration and relative [^{85}Sr]-microsphere blood flow. This is illustrated in Figure 2, which presents the data obtained for the kidneys of the same dog that produced the results of Figure 1. A large perfusion gradient naturally exists in the normal kidney, with the outer cortex receiving approximately three times the blood flow of the inner cortex (Slotkoff, *et al., Circ. Res.* 28:158-166; 1971). While in our study these anatomical regions were not rigorously separated during kidney dissection, the tissue samples obtained from each animal were nevertheless found to afford a good range of renal blood flow values.

CONCLUSIONS

The results of this study support the hypothesis that copper-62 labeled Cu(PTSM) could serve as a blood flow tracer for PET studies of the heart and kidney. Further work is in progress to better define the relationship between regional perfusion and the tissue radiocopper concentrations afforded by this radiopharmaceutical.

Diamox Enhanced Evaluation of Carotid Artery Disease Before and After Endarterectomy.

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Patients undergoing carotid endarterectomy were imaged after cerebral vasodilation before and after surgery using ^{123}I-iodoamphetamine (IMP) immediate and delayed SPECT imaging. One gram of Diamox (acetazolamide) was administered intravenously 25 minutes prior to injection of the IMP. SPECT imaging was begun 10 minutes later and repeated after 4 to 6 hours.

Preoperatively 3 patterns of IMP cerebral distribution were found: 1. interhemispheric or regional asymmetry which cleared on delayed imaging indicating depleted regional perfusion reserve and/or cerebral "steal", 2. focal decreases which did not clear (stroke), and 3. symmetric distribution.

Postoperative Diamox enhanced studies also showed 3 patterns: 1. normalization of previously asymmetric distribution, 2. increased uptake in the operated side with previous preoperative symmetric distribution, and 3. unchanged.

Clearing asymmetries or increased uptake after surgery identifies patients who had exhausted the capacity to maintain or increase global or regional cerebral blood flow either by collaterals or vasodilation. Preliminary clinical data indicates these patients benefit from endarterectomy.

Imaging Diamox responsiveness may not correlate to the usual ultrasound or angiographic anatomic data on severity of stenosis but adds unique and likely prognostic information about the hemodynamic effects of stenosis on the cerebral circulation.

THYROID SCAN AND/OR FINE NEEDLE ASPIRATION (FNA) IN THE EVALUATION OF SOLITARY THYROID NODULES. J. E. Freitas, H. J. Dworkin and C. E. Nagle. William Beaumont Hospitals, Royal Oak and Troy, MI.

To determine the value of radionuclide thyroid scanning in the evaluation of the solitary thyroid nodule in our referral population, 40 consecutive patients (31F, 9M) were studied who fullfilled the following criteria: (1) palpable solitary thyroid nodule, (2) nodule size and location amenable to biopsy, (3) current high-quality Tc 99m pertechnetate or I-123 pinhole thyroid scan, and (4) signed informed consent. All patients underwent neck palpation and FNA of the solitary nodule (size range 1.0-4.5 cm, mean 2.1 cm) prior to review of the thyroid scan. Scan findings of the 40 nodules were: 35 cold, 3 indeterminate, and 2 hot. Cytologic findings were: 3 positive for malignancy, 6 suspicious, 26 colloid nodules, 3 follicular adenoma, 1 Hashimoto's thyroiditis, and 1 non-diagnostic. Upon review of the thyroid scan immediately following the biopsy, only 2 scans (both hot nodules) were felt to provide clinically useful information that would have obviated or redirected the FNA. Thus, review of the scan prior to FNA is not necessary to adequately sample the nodule by FNA, but obviates the necessity of FNA in 5% of nodules. Previous work has demonstrated frequent suspicious cytologies in hot nodules, but both hot nodules in this small series exhibited benign follicular cytology. Following FNA, thyroid scanning would appear indicated in those nodules with suspicious cytology or in those patients in whom exogenous thyroid hormone suppression was desired.

PERFORMANCE OF Tc-99m DTPA AEROSOL LUNG SCANS ON VENTILATOR PATIENTS. R.M. McGraw, J.E. Juni and C.E. Nagle. William Beaumont Hospital, Troy, MI.

Diagnosis of pulmonary embolism in intensive care patients is a frequent challenge. Not only are the patients difficult to position for radionuclide imaging, but such patients are often receiving mechanical ventilation via an endotracheal (ET) tube. We have developed a technique for performance of Tc-99m-DTPA aerosol ventilation scans in such patients which results in both good tracer delivery and minimal release of aerosol into the environment.

A commercially available nebulizer (Mallinckrodt) is loaded with 60-90 mCi of Tc-99m-DTPA in 3 cc normal saline. The patient's respirator tubing is connected to a standard air-driven check valve which is, in turn, connected directly to a milliport filter. This filter is attached directly to the proximal end of the nebulizer with a separate supply of oxygen directed into the nebulization chamber. The distal end of the nebulizer is connected to a 100 cc piece of connecting tubing which is connected directly to the patient's endotracheal tube. The respirator is adjusted to allow for the additional 100-200 cc dead space. The oxygen supply to the nebulizer is started only after the above connections are complete. We have found that 5-10 minutes of ventilation with this apparatus is sufficient to deliver 3-5 mCi of aerosol to the lung beds.

By attaching the milliport filter in a position distal to the check valve, aerosol is prevented from entering room air or contaminating the respirator apparatus. Upon completion of the study, the oxygen to the nebulizer is first turned off. After a 2-3 minute waiting period to eliminate residual aerosol in the tubing, the nebulizer is disconnected from the patient and the tubing proximal to the milliport filter is reconnected directly to the ET tube. Total time to connect or disconnect is less than 1 minute.

In summary, we have described a methodology for reliably obtaining aerosol ventilation scans of respirator patients which is conceivable, effective, and avoids contamination of room air or respiratory apparatus.

DECONVOLUTIONAL ANALYSIS OF HEPATOBILIARY SCANS IN THE JAUNDICED INFANT.

G. Gora, J.E. Juni, R. Holmes.
William Beaumont Hospital, Royal Oak, Michigan

Visual interpretation of hepatobilary scans in neonates is challenging and often indeterminate. Early diagnosis is key to effective management. We have studied the use of deconvolutional analysis (DCA) of hepatobilary scans in neonates with jaundice of unknown etiology.

10 infants (median age 33 days) recieved 70 μCi/kg Tc-99m-mebrofenin or disofenin iv after 5 day pre-treatment with 5 mg/kg phenobarbitol. Imaging began 1 min prior to injection and continued for 30 mins with computer acquisition at 60 sec/frame. Time activity curves for heart and liver were subjected to DCA for calculation of hepatic extraction fraction (HEF). Static images were obtained for 24 hours or until visualization of gut activity. Final diagnosis was established by liver biopsy and/or long-term clinical follow-up.

Results were as follows (TNJ = transient neonatal jaundice, α-1 = α-1-antitrypsin deficiency, BA = biliary atresia, TPN = TPN induced hepatitis):

#pts	Dx	total bilirubin / avg	HEF / avg
5	TNJ	3.4-13.6 / 7.0	79-100 / 90%
2	α-1	7.8,9.1 / 8.45	60, 83 / 71.5%
1	BA	7.0	61%
2	TPN	6.5,22 / 14.5	14,25/ 19.5%

Visual appearance of scans was non-contributory. DCA aids the differential diagnosis of the jaundiced infant, especially by identification of self-limited liver disease.

PROSTATIC SPECIFIC ANTIGEN (PSA) AND BONE SCANNING IN FOLLOW-UP OF PROSTATE CANCER PATIENTS S/P DEFINITIVE THERAPY. R. P. Gilvydis, J. E. Freitas, J. D. Ferry, D. C. Blake, and J. A. Gonzalez. William Beaumont Hospital, Royal Oak MI.

To assess the value of PSA, a new immunoradiometric (IRMA) assay specific for prostate tissue, in prostate cancer follow-up, 107 consecutive patients were studied who fulfilled the following criteria: 1) pathologic diagnosis of prostate cancer; 2) definitive therapy by prostatectomy and/or radiation therapy at least three months prior; and, 3) Tc-99m methylene diphosphate bone scan and PSA sampling within three months of each other. The mean follow-up since definitive therapy was 1.5 years. All bone scans were correlated with available radiographs, and the presence or absence of metastatic bone disease determined. Of the 107 bone scans, 16 demonstrated metastatic bone disease. The PSA concentration (ng/ml) and bone scan findings for metastatic bone disease are shown:

		PSA Concentrations		
		≤8	>8 <40	≥40
Bone Scans	+	1	6	9
	-	67	15	9

Thus, a PSA value of ≤8 ng/ml (derived from ROC curve analysis) excludes the presence of metastatic bone disease with a predictive value of a negative test of 98.5% ($P<0.001$). As the PSA value increases further, the probability of metastatic bone disease also increases (>8 ng/ml, 38.4%; >10 ng/ml, 60%). In summary, bone scanning in prostate cancer follow-up after definitive therapy is not routinely indicated if the PSA value is ≤8 ng/ml because of its low yield.

TWO-STAGE RADIONUCLIDE CYSTOGRAPHY: EARLY RESULTS. R.V. Posderac, C.J. Becker, C. Reitelman, and L.R. Kuhns. Children's Hospital of Michigan and Wayne State University School of Medicine, Detroit, Michigan.

The advantages of radionuclide cystography (RNC) over voiding cystourethrography include a higher sensitivity for the detection of vesicoureteral reflux (VUR) and a significant reduction in radiation exposure to the patient. It is known that continuous antibiotic prophylaxis in children with a history of urinary tract infection and VUR is more effective than intermittent antibiotic therapy for prevention of renal scarring. Cessation of antibiotic prophylaxis has been advocated by some clinicians when a single normal radionuclide cystogram has been documented in these patients. The purpose of the present study was to evaluate whether Two-stage RNC has advantages over a single stage study and whether further evaluation of this technique is warranted.

Twenty-five children (23 females, 2 males; age range 4 months-18 years with a mean of 8.0 years) suspected of VUR had Two-stage RNC which consisted of a repeat study performed immediately following completion of routine (single stage) RNC. Our routine RNC consists of "feeding tube" catheterization of the urinary bladder and measurement of residual volume after pretest voiding, instillation of 1 mCi Tc-99m pertechnetate followed by pre-warmed normal saline infusion to patient tolerance, and continuous computer acquisition during the filling, voiding, and post-voiding phases; the second stage of Two-stage RNC is similarly performed except the feeding tube catheter remains in place between the two stages.

Maximum bladder volumes achieved on the second stage of Two-stage RNC were equal to or greater than those achieved on the first stage in 21 patients and exceeded the first stage volumes in 14 patients by 7-60% (mean 24%). Only in 2 children older than 2 years of age did the maximum bladder volume on the first stage exceed that attained on the second stage.

VUR was identified in 13 patients. Major discrepancies between the two stages included: (a) reflux identified only on 2nd stage in two patients, (b) reflux identified only on 1st stage in one patient, (c) unilateral reflux identified on both stages involved opposite kidneys in one patient, (d) bilateral reflux identified on one stage but was unilateral on the other stage in two patients.

These results indicate that further evaluation of Two-stage RNC in additional patients is warranted. The procedure may prove to be of clinical value for physicians requiring one normal RNC examination before discontinuing antibiotic prophylaxis; it may also warrant consideration for adoption as a routine method for the performance of RNC.

ENHANCEMENT OF INDIUM-111 WBC SCANS OF HEMODIALYSIS FISTULAS BY TECHNETIUM-99m RBC SUBTRACTION. E.C. Schane, J.E. Juni and C.E. Nagle. William Beaumont Hospital, Troy, MI.

Infection of hemodialysis fistulas (shunts) may be difficult to diagnose. If not promptly treated it may progress to sepsis with significant morbidity or mortality. In-111 white blood cell scans have been used in this setting but are frequently difficult to interpret due to normal blood pool activity of In-111 white blood cells in the fistula. In order to separate normal blood pool activity from abnormal white blood cell accumulation, we have developed a technique using dual isotope scanning with Tc-99m red blood cells.

Whole body In-111 white blood cell imaging is first performed within 24 hours after in vitro labeling and administration of 500 uCi of In-111 white blood cells. Sn++ PYP, (14.7 ug per kg body weight to maximum dose of 1000 ug) is injected just prior to taking the 24 hour image. If additional images are desirable they should be obtained prior to immobilizing the fistula site. A static 100K count In-111 white blood cell image of the fistula site is then obtained with both analog and 128 x 128 byte mode computer acquisition. Immediately following this, the patient is injected in the opposite extremity with 5 mCi Tc-99m pertechnetate for in vivo red blood cell labeling. Analog and computer images of the immobilized fistula are again obtained for 100K using a 140 kev window.

The analog In-111 white blood cell and Tc-99m red blood cell images are acquired on separate film for comparison and can be overlayed to identify the blood pool component of the fistula image. The Tc-99m red blood cell image is then computer subtracted from the In-111 white blood cell image after count normalization.

We have found the In-111 white blood cell blood pool activity is frequently seen in hemodialysis fistulas, making detection of infection of these sites difficult. The use of Tc-99m red blood cell subtraction to identify blood pool activity enhances the interpretation of these images.

ANALYSIS OF HUMAN ANTIMURINE MEDIATED IMMUNOGLOBULIN COMPLEX FORMATION IN PATIENTS RECEIVING MURINE MONOCLONAL ANTIBODIES. A.M. Zimmer, J.M. Kazikiewicz, R. Goldman-Leikin, E.H. Kaplan, D.I. Webber, B.A. Patel, W.G. Spies, S.M. Spies, and S.T. Rosen. Northwestern University Medical Center, Chicago, IL.

Radioimmunotherapy retreatment of patients receiving radiolabeled monoclonal antibodies is difficult due to human antimurine antibody formation. Analysis of HAMA mediated immunoglobulin complex formation was performed on serum samples of patients receiving radioiodinated murine monoclonal antibodies T101 and B72.3 prior to and following immunotherapy retreatment. Size exclusion HPLC analysis, immunoreactivity, and animal biodistribution studies were conducted with in vitro formed radiolabeled antibody-antibody immunoglobulin complexes. Results of the study showed high liver uptake with low blood activity and significant losses in immunoreactivity with high molecular weight radioimmune complexes greater than 1250 Kdaltons. With intermediate molecular weight radioimmune complexes (450 -970 Kdaltons), animal biodistribution data showed low liver uptake and high blood activity with minor losses in immunoreactivity. Slow addition of radiolabeled antibody to HAMA samples reduced radioimmune complex formation and increased immunoglobulin size. No further complexing of additional radiolabeled antibody to preformed in vitro immunoglobulin complexes was observed. The effect of plasmapheresis on HAMA titers in patients prior to immunotherapy retreatment was further evaluated. Plasmapheresis significantly reduced HAMA titers in all patients treated. Using plasmapheresis and/or antibodies, our laboratory has successfully removed circulating HAMA from patients prior to retreatment.