mation on the pharmacokinetic changes caused by a particular amino acid regimen is needed. Renal uptake of radiometals from radioconjugates could be influenced, at least to some extent, by the glomerular filtration rate, urinary flow rate, urinary pH and solute and protein/amino acid concentrations. A significant degree of aminoaciduria should occur in the amino acid treated patients if treatment with amino acids saturates the absorptive mechanisms, either by blocking the negative tubular membrane charges or by blocking specific receptors (or both). Thus, at a "blocking" dose, the urine should demonstrate increase in excretion of both radioconjugate and non-radioactive infused amino acids. Urinary amino acid profiles could, therefore, be correlated with inhibition of tubular absorption as well as decreased intracellular metabolism of filtered radioconjugates.

CONCLUSION

The multiplicity of variables make it difficult to predict the effect of the experimental manipulation a priori. The hypothesis and preliminary work in animals and patients suggesting that an amino acid infusion mixture results in decreased tubular absorption of peptides and small radioimmunoconjugate proteins is certainly worthy of further study. Only a modest reduction in renal uptake was found in this initial clinical study (*16*), but the results are interesting and the implications of potentially great importance. Additional clinical trials with documentation of renal function, and quantitative amino acid and protein excretion profiles for radioactive and nonradioactive species in the baseline and postinfusion urine, are warranted. Knowledge of ways to decrease renal uptake of radiometals would be invaluable for tumor scintigraphy and targeted radiotherapy.

Sally J. DeNardo
Robert T. O'Donnell
Gerald L. DeNardo
University of California
Sacramento, California
Veterans Administration Northern California
Healthcare System
Sacramento, California

REFERENCES

1. Behr TM, Becker WS, Bair HJ, et al. Comparison of complete versus fragmented technitium-99m-labeled anti-CEA monoclonal antibodies for immunoscintigraphy in colorectal cancer. *J Nucl Med* 1995;36:430–441.
2. Baum RP, Niesen A, Hertel A, et al. Initial clinical results with technetium-99m-labeled LL2 monoclonal antibody fragment in the radioimmunodetection of B-cell lymphomas. *Cancer* 1994;73:896–899.
3. Krenning EP, Bakker WH, Kooij PP, et al. Somatostatin receptor scintigraphy with indium-111-DTPA-D-Phe-1-octreotide in man: metabolism, dosimetry and comparison with iodine-123-tyr-3-octreotide. *J Nucl Med* 1992;33:652–658.
4. Behr T, Becker W, Hannappel E, Goldenberg DM, Wolf F. Targeting of liver metastases of colorectal cancer with IgG $F(ab')_2$, and FAB' anti-CEA antibodies labeled with ^{99m}Tc: the role of metabolism and kinetics. *Cancer Res* (suppl) 1995:5777S–5785S.
5. Buijs WCAM, Massuger LFAG, Claessens RAMJ, Kenemans P, Corstens FHM. Dosimetric evaluation of immunoscintigraphy using indium-111-labeled monoclonal antibody fragments in patients with ovarian cancer. *J Nucl Med* 1992;33:1113–1120.
6. Silbernagl S. The renal handling of amino acids and oligopeptides. *Physiol Rev* 1988;68:912–986.
7. Maack T, Johnson V, Kan ST, Figueiredo J, Sigulem D. Renal filtration, transport and metabolism of low molecular weight proteins: a review. *Kidney Int* 1979; 16:251–270.
8. Duncan JR, Welch MJ. Intracellular metabolism of indium-111-DTPA-labeled receptor targeted proteins. *J Nucl Med* 1993;34:1728–1738.
9. Motta-Hennessy C, Sharkey RM, Goldenberg DM. Metabolism of indium-111-labeled murine monoclonal antibody in tumor and normal tissue of the athymic mouse. *J Nucl Med* 1990;31:1510–1519.
10. Kirk E. Studies on the amino acid clearance. *Acta Med Scand* 1936;89:450–453.
11. Morgenson CE, Sölling K. Studies on renal tubular protein re-absorption: partial and near complete inhibition by certain amino acids. *Scand J Clin Lab Invest* 1977;37:477–486.
12. Pimm MV, Gribben SJ. Prevention of renal tubule re-absorption of radiometal (indium-111) labeled Fab fragment of a monoclonal antibody in mice by systemic administration of lysine. *Eur J Nucl Med* 1994; 21:663–665.
13. Behr TM, Sharkey RM, Juweid ME, Aninipot R, Goldenberg DM. Reduction of the kidney uptake of Fab' fragments of monoclonal antibodies: animal experimental and initial clinical results [Abstract]. *Proc Am Assoc Cancer Res* 1995;86:617.
14. Behr TM, Sharkey RM, Juweid ME, et al. Reduction of the renal uptake of radiolabeled monoclonal antibody fragments by cationic amino acids and their derivatives. *Cancer Res* 1995;55:3825–3834.
15. Hammond PJ, Wade AF, Gwilliam ME, et al. Amino acid infusion blocks renal tubular uptake of indium-labelled somatostatin analogue. *Br J Cancer* 1993;67: 1437–1439.
16. Behr TM, Becker WS, Sharkey RM, et al. Reduction of the renal uptake of monoclonal antibody fragments by amino acid infusion: initial clinical results. *J Nucl Med* 1996;37:829–833.

Exercise Renography in Untreated Subjects with Essential Hypertension

Eugene J. Fine, M. Donald Blaufox, Jon D. Blumenfeld, John H. Laragh, Kwang J. Chun, Sherman L. Heller and Josephine A. Bongiovanni
Department of Nuclear Medicine, Montefiore Medical Center, Moses Division, The Albert Einstein College of Medicine; and Department of Medicine, Cornell University Medical Center, Ithaca, New York

Exercise induced renal dysfunction is reported to occur in treated hypertensive patients but not seen normotensive subjects. It is unclear if this phenomenon is related to the disease or to treatment. **Methods:** Four normal volunteers and 15 hypertensive subjects (antihypertensive medications were discontinued for more than 4 wk) were studied with upright radionuclide renography at rest and during bicycle exercise. The amount of exercise was sufficient to increase the heart rate at least 20 bpm above the resting value. All subjects were healthy, without evidence of left ventricular hypertrophy renal disease or hypertensive retinal disease. BUN, serum creatinine concentration and urinalysis were normal in all subjects. Renograms were performed for 12–15 min after injection of either 1 mCi [^{123}I]orthoiodohippurate (OIH) or 2–7 mCi ^{99m}Tc-mercaptoacetyltriglycine (MAG3). Visual analysis and mean transit time calculation were performed on the rest and exercise studies. **Results:** Seven of 14 hypertensive subjects and none of the normal volunteers demonstrated abnormal prolongation in renal transit during exercise which was not seen on the resting renogram. Four of these seven subjects had a history of hypertension for 2 yr or less. **Conclusion:** About 50% of individuals with mild-to-moderate hypertension and normal renal function may have abnormal renal transit of renal excretion agents during exercise, although their baseline studies are normal. This finding is unassociated with therapy and appears to be related directly to the pathophysiology of essential hypertension.

Key Words: renal hypertension; iodine-123-OIH; technetium-99m-MAG3; renal circulation

J Nucl Med 1996; 37:838–842

Received Mar. 10, 1995; revision accepted Oct. 8, 1995.
For correspondence or reprints contact: Eugene J. Fine, MD, Bronx Municipal Hospital Center, Nuclear Medicine Department, Jacobi Hospital BN13, Pelham Pkwy. and Eastchester Rd., Bronx, NY 10461.

Clorius et al. (*1*) described exercise-induced renal dysfunction in treated hypertensive subjects. They reported unilateral or bilateral prolongation in renal parenchymal transit studied with hippuran renography during exercise in 57% of subjects. All other measures of renal function, including a resting hippuran renogram, were normal in these patients. No attempt to control for antihypertensive medication was made. Renographic abnormalities, therefore, may have been related to antihypertensive medications, which are well-known to cause changes in renal function. Alternatively, the abnormal findings may have been related to the underlying pathophysiology of hypertension.

Recent hypotheses to explain the pathophysiology of uncomplicated essential hypertension (*2,3*) postulate abnormal afferent arteriolar vasoreactivity in patients with essential hypertension, which is not present in normotensive individuals. This reaction may be responsible for the chronic excess salt and water reabsorption characteristic of this disease.

One such hypothesis (*2*) suggests that focal afferent arteriolar spasm results in focally elevated renin secretion causing inappropriate hyperreninemia. This results in net increased salt and water reabsorption by the remaining adaptive nephrons and increased flow and hyperfiltration, as well as suppression of plasma renin activity. A related hypothesis (*3*) suggests that there is abnormal cortical renin sensitivity leading to renin-mediated reduction of afferent arteriolar blood flow of cortical nephrons. This would result in greater salt and water reabsorption in these nephrons. Enhanced sodium and water reabsorption, presumably subtle at rest, would also explain prolonged renal transit, especially if the prolongation is enhanced by exercise, an intervention known to reduce renal blood flow.

In later studies, Clorius et al. (*4*) showed that the effects of antihypertensive medications were statistically unlikely to be related to the abnormal renographic findings on exercise images. The implication for a potential pathogenic link to essential hypertension in more than 50% of individuals, however, provided the stimulus for the present investigation. It is important to determine definitively if this phenomenon occurs in patients in whom antihypertensive medications have been discontinued.

MATERIALS AND METHODS

Four normal volunteers and 15 hypertensive subjects were included in the study. Eligible hypertensive subjects were referred from the Cornell Cardiovascular Center to Department of Nuclear Medicine, Montefiore Medical Center, where exercise renography was performed. Patients were selected with mild-to-moderate hypertension (diastolic BP of 90–105 mmHg, and systolic BP <180 mmHg). Radiographic evidence of cardiomegaly and electrocardiographic evidence of LVH were absent. BUN and serum creatinine were required to be less than 20 mg/dl and 1.3 mg/dl, respectively. Individuals with proteinuria were excluded. Patients also excluded were those who had evidence of hypertensive retinopathy. These requirements were necessary to reduce the likelihood of hypertensive end-organ vascular damage, which might be responsible for the exercise-induced changes.

All antihypertensive medications were discontinued for at least 4 wk and the patients were placed on a no-salt-added diet prior to the study. Only juice, toast and decaffeinated coffee were allowed on the morning of the examination to minimize potential differences in renal function due to diet. Liquids were administered by mouth 30 min prior to the examination (250–500 ml). An intravenous line was placed in the brachial vein to assure hydration and facilitate blood sampling. The resting heart rate was required to be less than 90 bpm.

All normal and hypertensive subjects signed a written informed consent form, approved by the institutional review boards of both collaborating institutions.

Imaging Protocol

A large field of view gamma camera interfaced to a computer was used with high-resolution low-energy collimation. Exercise was performed on a stationary bicycle. The first 10 subjects were studied with [^{123}I]orthoiodohippurate (OIH). During this portion of the study, ^{99m}Tc-MAG3 was not yet commercially available. When MAG3 became commercially available, however, we switched to this radiotracer to utilize the improved statistics provided by higher usable doses of this tracer. OIH (1 mCi) was administered with the rest portion of the study and then again during exercise renography. For the MAG3 study, 2 mCi were administered at rest and 7 mCi during exercise.

Patients were positioned upright on a stationary bicycle in the posterior projection, with the heart and kidneys in the field of view. Computer acquisition was set for 5 sec/frame and was continued for 12–15 min during both the resting and exercise portions of the exam.

After the baseline renogram, the patient rested for 45 min. Blood samples were obtained in six hypertensive subjects 45 min after the resting injection of MAG3 to determine MAG3 clearance and effective renal plasma flow (ERPF) (*5,6*).

The first 10 subjects were studied using the protocol of Clorius et al. (*1*), which prescribed a target exercise heart rate of 20 bpm over the baseline rate. The exercise protocol was altered in the remaining nine (MAG3) subjects to achieve a target of 60% of the maximum predicted heart rate (MPHR), according to standard tables based upon age and sex (*7,8*). We also wanted to individualize the work load for each subject more accurately than in the original protocol. The tracer bolus during exercise was given at the attained heart rate. Heart rate and blood pressure were monitored every 2 min.

Computer matrix images were used to derive manual whole kidney and heart regions of interest (ROIs). From these ROIs, a nonbackground subtracted renogram and cardiac time-activity histogram curves were generated. Renal mean transit time (MTT) was calculated in all subjects after deconvolution of the renogram was performed using the heart curve as the input function (*9*).

Abnormal Renal Transit

Differences in MTT between exercise and rest studies were determined from the normal volunteers to determine the range of normal differences. Quantitatively prolonged transit was defined from this normal set; the value was calculated as the mean difference in MTT between exercise and rest among the normal subject kidneys, plus 2 s.d. of the mean. Abnormal transit was defined as prolongation of the MTT by the above quantitative criterion or visual prolongation of transit on the scintigram, or both.

Statistical Analysis

Renal functional measures (BUN, serum creatinine concentration, creatinine clearance, effective renal plasma flow, plasma renin activity), age and duration of hypertension were compared in subjects with and without abnormal transit. Comparisons were made by pooled t-tests, and by nonparametric testing for pooled samples (Mann-Whitney U-test).

RESULTS

One normal subject and one hypertensive subject were excluded from further evaluation due to vasovagal responses during baseline renography while sitting upright on the bicycle. Hemodynamic parameters are indicated in Table 1. It should be noted that the four normal subjects were studied with OIH. Moreover, the hypertensive subjects who had MAG3 tests achieved a higher mean heart rate than did the first 10 subjects

TABLE 1
Hemodynamics

Rest	Exercise
Normal subjects (OH) (n = 3)	
BP (mmHg) (112 ± 11)/(77 ± 13)	(122 ± 10)/(82 ± 2)
HR (bpm) 74.7 ± 10.2	95.8 ± 8.0
Hypertensive subjects (OIH) (n = 6)	
BP (156 ± 11)/(104 ± 17)	(168 ± 16)/(118 ± 11)
HR 73.0 ± 6.2	96.2 ± 16.8
Hypertensive subjects (MAG3) (n = 8)	
BP (147 ± 10)/(98 ± 7)	(183 ± 18)/(97 ± 10)
HR 68.0 ± 10.6	119.5 ± 16.0

(four normals, six hypertensives) studied with OIH, as expected, because of the study design.

No kidneys among our normal subjects showed prolonged transit with exercise. Bilateral abnormal transit was observed (50% of patients and kidneys) in seven hypertensive subjects (Table 2). Three of these subjects were studied with OIH and four with MAG3. The mean change in transit time in the control group was 8.2 ± 12.4 sec. The hypertensive subjects had a mean change in transit time of 31.3 ± 37.1 sec, which is not significantly different ($p > 0.2$) in a pooled comparison from the control value.

TABLE 2
Change in Transit Time (sec)

	R Kidney	L Kidney	Qualitative scintirenogram	Comments
Normal Subjects (OIH)				
1	(−61)	(−34)	−	Excluded*
2	10	6	−	
3	3	−12	−	
4	21	21	−	
Mean ΔTT = 8.2 ± 12.4 sec (n = 6 kidneys)				
Hypertensive subjects (OIH)				
5	9	12	−	
6	33	40	+	
7	9	14	−	
8	12	−20	−	
9	31	28	+	
10	93	91	+	
Mean ΔTT = 29.3 ± 33.1 sec (n = 12 kidneys)				
Hypertensive subjects (MAG3)				
11	−3	3	−	
12	9	7	−	
13	−5	−22	−	
14	93	86	+	
15	48	107	+	
16	34	75	+	
17	−2	−4	−	
18	52	48	+	
19	np	np	np	Excluded*
Mean ΔTT = 32.9 ± 40.8 (n = 16 kidneys)				
Mean ΔTT for all kidneys for all hypertensive subjects = 31.3 ± 37.1 sec				

*Both patients excluded experienced vasovagal reactions during the baseline study.
np = not performed.

Table 3 indicates the study results along with renal function parameters, age and duration of hypertension at the time of the study. The mean duration of hypertension among subjects with positive exams was 7.3 yr ± 7.0 (s.d.) with no significant difference ($p > 0.2$) compared with individuals with negative exams (duration 14.3 yr ± 14.3). Four of the positive exams were among subjects whose duration of hypertension was 2 yr or fewer. The ERPF was 337 ml/min in subject 18 (Table 3). All other measures of renal function were normal in this individual. Additionally, all measures of renal tubular and glomerular function were normal in all other subjects studied. There were no statistically significant differences between subjects with positive and negative exams.

Positive studies (i.e., normal at rest, abnormal transit during exercise) are demonstrated in Figures 1 (OIH study) and 2 (MAG3 study). Clearly prolonged parenchymal transit is observed scintigraphically as well as renographically in each study during exercise. The lower panel of each figure demonstrates a qualitative difference in the deconvolved renogram of the exercise study compared to the baseline resting study.

DISCUSSION

Our results demonstrate abnormal renal transit during upright bicycle exercise not seen during rest in 7 of 14 individuals with essential hypertension and normal renal function. Four normotensive controls demonstrated normal renal transit during exercise. These results confirm the findings of Clorius et al. (*1,4*) and extend them to unmedicated hypertensive subjects.

Examples of prolonged transit include bilaterally delayed excretion of radiographic contrast in the intravenous urogram (IVU) of dehydrated patients and unilateral delay in patients with renal artery stenosis (on the stenotic side). The subtle degrees of prolonged transit expected in essential hypertension by the above hypotheses, however, require more sophisticated techniques than the IVU. Both the hypothesis of focal nephron ischemia (*2*) and abnormal cortical vasoconstriction (*3*) suggest the possible presence of a distinct small subpopulation of abnormal nephrons, as compared to a larger population of normal nephrons. Larger groups of abnormally vasoactive nephrons cannot be excluded in some individuals or a continuum of graduated vasoactivity among the total nephron population. Prolonged transit due to such populations of nephrons, in general, may not be observable without provocative maneuvers.

Physiologic interventions may be expected either to exaggerate or to attenuate the prolongation in transit time depending on the actual mechanism of intrarenal abnormality. For example, reduced renal blood flow would be expected to increase renal renin secretion. It would be presumptious at this point to predict the precise relation of transit time to flow in hypertensive patients compared to normal control subjects, but the following pattern of response would be reasonable: At normal to slightly subnormal flow rates, renal transit time would not be perceptibly different between hypertensives and controls. At the extreme of marked flow reduction, maximum renin secretion would prolong transit time equally in normal subjects and hypertensive individuals. At intermediate flow reduction, however, increased sensitivity to flow reduction in hypertensive individuals would distinguish them from normotensive controls, whose intact autoregulatory mechanisms would prevail. We would expect prolongation in transit time in hypertensive individuals at renal flow reductions which provoke no such prolongation in normal controls.

Interventions that are known to reduce renal blood flow include upright posture, exercise (*10*), dehydration (*11*) and numerous medications. Several investigators have reported

TABLE 3
Study Results and Renal Function Parameters at Time of Study

Subject no.	Study result	Age (yr) at study	Duration (yr) HTN at study	BUN (mg/dl)	Serum creat. (mg/dl)	Creatinine clearance (ml/dl)	Plasma renin activity	ERPF (ml/min)	Comment
5	−	42	4	9	1.4	137	−	−	OIH
6	+	50	2	18	1.0	105	−	−	OIH
7	−	50	18	17	1.1	NP	−	−	OIH
8	−	51	12	14	1.1	84	−	−	OIH
9	+	39	0.2	14	1.2	107	−	−	OIH
10	+	56	1.7	15	1.2	134	−	−	OIH
11	−	59	41	16	1.3	112	1.9	NP	MAG3
12	−	23	2	12	1.1	131	4.4	604	MAG3
13	−	33	6	13	0.8	145	4.1	604	MAG3
14	+	33	12	14	0.9	121	4.7	649	MAG3
15	+	39	18	9	1.0	NP	0.5	799	MAG3
16	+	34	10	11	0.8	124	0.4	NP	MAG3
17	−	59	8	20	1.1	119	0.3	559	MAG3
18	+	42	2	18	0.6	128	4.1	337	MAG3
Mean study	+	42.0 ± 9.6	7.3 ± 7.0	14.1 ± 3.7	0.9 ± 0.2	122.4 ± 10.9	2.4 ± 2.3	595 ± 236*	
Mean study	−	45.4 ± 13.6	14.3 ± 14.3	14.4 ± 3.6	1.1 ± 0.2	121.3 ± 21.8	2.6 ± 1.9	589 ± 26*	

*Not significant; all comparisons $p > 0.2$ by Mann Whitney U-test and pooled t-test.
+ = prolonged transit; NP = not performed.

transit time prolongation upon provocative maneuvers in hypertensive subjects.

In 1983, Clorius and Schmidlin (*1*) described the "exercise renogram" in which participants were injected twice with [^{131}I]OIH, once prone at rest, and on a second day after bicycle exercise (sufficient to raise the heart rate >20 bpm over baseline values). Twenty-nine of 51 (57%) subjects demonstrated exercise-induced prolonged renal transit. Fifteen normotensive volunteers were also studied and did not demonstrate exercise induced renal dysfunction. Antihypertensive medications were not discontinued and no attempt was made either to characterize or control for the subjects' pharmacologic state. The nature of the clinical referral base did not permit the study of patient's withdrawn from medication. This design flaw compromised interpretation of exercise-induced prolonged renal transit since antihypertensive medications may profoundly affect renal hemodynamics. Clorius and Schmidlin partially redressed this deficiency in a subsequent study (*4*) in which multiple logistic regression analysis revealed no statistical relation between medication and transit prolongation during exercise. The observation was important since it supported the concept of abnormal renal vascular responsiveness in a high percentage of individuals with essential hypertension.

The role of the renal vasculature in abnormal autoregulation in essential hypertension was further supported in later investigations. Whereas exercise causes ERPF to fall in excess of glomerular filtration rate during exercise in normal subjects (*10*), this relation may not hold in hypertensive individuals. Clorius et al. (*12*) indicated a fall in filtration fraction in subjects with hypertension. Gruenwald et al. (*13*) used pharmacologic intervention and found that: (a) Nadalol, compared with no intervention, caused no mean change in renal transit in hypertensive subjects, while (b) captopril restored flow toward normal transit.

It is not possible to completely exclude subtle, clinically undetectable hypertensive renal damage as the cause of our observation. Although we do not have renal biopsy data in these subjects, renal function was normal and did not differ in subjects with or without abnormal transit (Table 3).

An important concern about these observations is whether prolonged transit with exercise is restricted to hypertensive individuals. Clorius et al. (*1,12*) did not observe abnormal renal transit during exercise in 22 normotensive control subjects studied previously. We thought it unethical to study a large number of normal persons in view of these earlier reports. Our study of normal subjects, therefore, was limited to only four. Complete evaluation of MTT was possible in three of them. The fourth control subject who had a vasovagal response during baseline renography was noted to have normal renal transit during exercise. Therefore at least 26 normotensive subjects have been studied with exercise renography and none have had prolonged transit. Therefore, the occurrence of exercise-induced renal dysfunction in normal subjects is extremely low and certainly not nearly as common as in hypertensive subjects.

It should be noted that Mizuiri et al. (*14*) reported exercise-induced renographic changes in 14 subjects, described as normotensive, with similar findings in 14 hypertensive subjects. The mean diastolic blood pressure, however, in their "normotensive group" was 93 ± 11 mmHg, a value clearly in the hypertensive range. The diastolic pressure of the normotensive group in the present study was 77 ± 13 mmHg. Therefore, we do not believe that Mizuiri et al. have shown this phenomenon to occur in normotensive individuals.

CONCLUSION

In this study, 7 of 14 subjects (50%) with mild-to-moderate hypertension and normal baseline studies demonstrated renal dysfunction during exercise. Prolonged renal transit during exercise therefore does not appear to be associated with medication and may relate to a primary renal mechanism of hypertension in a large subset of individuals with essential hypertension.

ACKNOWLEDGMENTS

We thank Joyce Rush for preparing the manuscript and Dr. Yi Li for his assistance in preparing the illustrations.

Supported in part by the National Institutes of Health grant P50 HL18323-19. Presented in part at the 38th Annual Meeting of the Society of Nuclear Medicine, Orlando, FL, June 8–12, 1994.

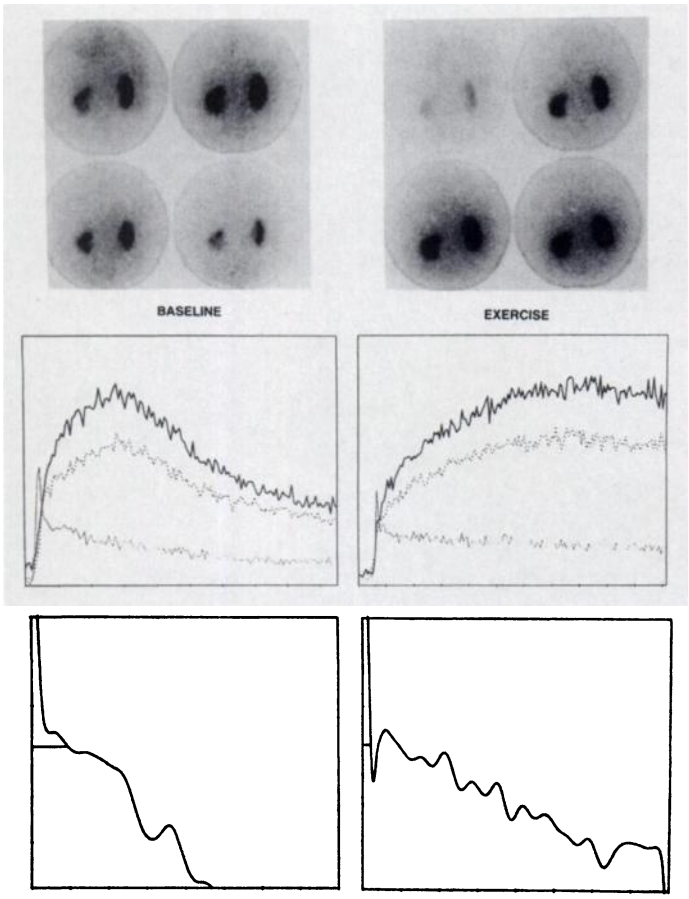

FIGURE 1. Rest scintigram in Subject 10, (top left panel, after administration of 1 mCi ^{123}I-OIH) shows slight renal asymmetry but otherwise normal appearance through 12 min. Deconvolved renogram for left kidney in lower left panel is normal. Right panel: 1 mCi OIH given during exercise shows progressive parenchymal accumulation for 12 min on scintigram and renogram. Deconvolved left renogram (lower right panel) shows prolongation of transit compared to the rest study (left).

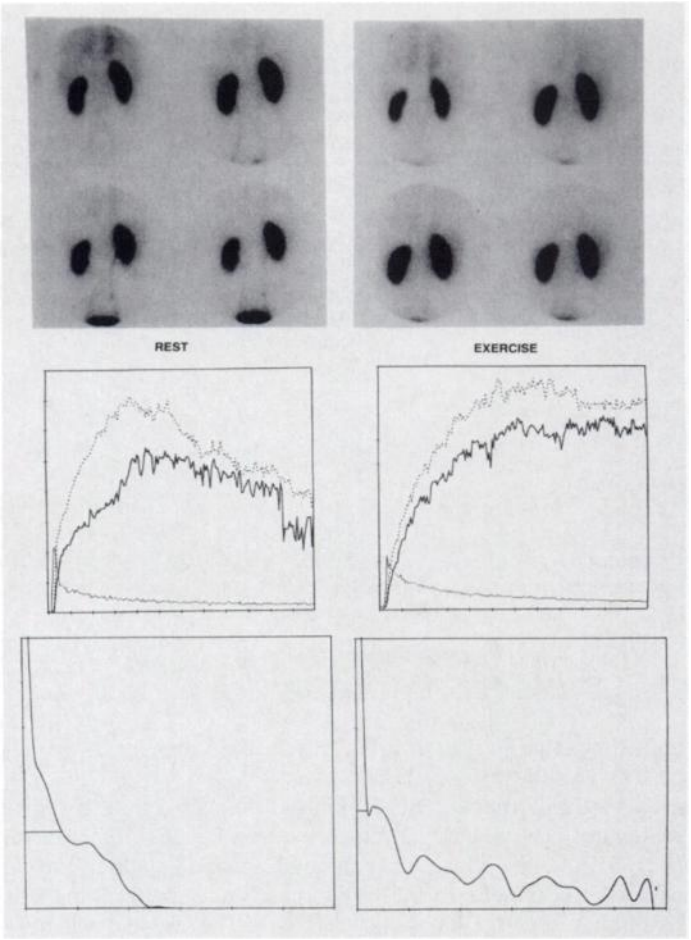

FIGURE 2. Subject 15 was studied at rest after injection of 2 mCi ^{99m}Tc-MAG3 (left) and during exercise with 7 mCi MAG3 (right). The 12-min studies show prolonged transit on exercise compared to rest study. Prolongation is more noticeable on the renograms (middle panels) and deconvolved renograms (bottom panel; left kidney only) than on the scintiscans.

REFERENCES

1. Clorius JH, Schmidlin P. The exercise renogram: a new approach documents renal involvement in systemic hypertension. *J Nucl Med* 1983;24:104–109.
2. Sealey JE, Blumenfeld JD, Bell GM, Pecker MS, Sommers SC, Laragh JH. On the renal basis for essential hypertension: Nephron heterogeneity with discordant renin secretion and sodium excretion causing a hypertensive vasoconstriction volume relationship. *J Hypertens* 1988;6:763–777.
3. Britton KE. Essential hypertension: a disorder of cortical nephron control? *Lancet* 1981;2:900–903.
4. Clorius JH, Mann J, Schmidlin P, Strauss LG, Saur T, Irngartinger G. Clinical evaluation of patients with hypertension and exercise-induced renal dysfunction. *Hypertension* 1987;10:287–293.
5. Tauxe WN, Dubovsky EV, Kidd T, Diaz F, Smith LR. New formulas for the calculation of effective renal plasma flow. *Eur J Nucl Med* 1982;7:51–54.
6. Taylor A Jr, Corrigan P, Eshima D, Folks R. Prospective validation of a single sample technique to determine technetium-99m-MAG3 clearance. *J Nucl Med* 1992;33:1620–1622.
7. Astrand I. Aerobic work capacity in men and women with special reference to age. *Acta Physiol Scand* 1960;49(suppl 169):7–92.
8. Astrand P, Rhyming I. A nomogram for calculation of aerobic capacity (physical fitness) from pulse rate during submaximal work. *J Appl Physiol* 1954;7:218–221.
9. Diffey BL, Hall FM, Corfield JR. The ^{99m}Tc-DTPA dynamic renal scan with deconvolution analysis. *J Nucl Med* 1976;17:352–355.
10. Castenfors J. Renal function during exercise. *Acta Physiologica Scandinavia* 1967; 70(suppl):7–44.
11. Crum CE, Luft FC, Fineberg MS, et al. Responses to volume expansion and constriction in categorized hypertensive and normotensive man. *Hypertension* 1979; 1:476–485.
12. Clorius JH, Reinbold F, Hupp T, Mandelbaum A, Schmidlin P, van Kaick G. Renovascular hypertension: a perfusion disturbance that escaped recognition. *J Nucl Med* 1993;34:48–56.
13. Gruenewald SM, Nimmon CC, Nawaz MK, Britton KE. A noninvasive gamma camera technique for the measurement of intrarenal flow distribution in man. *Clin Sci* 1981;61:385–389.
14. Mizuiri S, Hayashi I, Hirata K, Yamasaki J, Sasaki Y. Exercise-induced renal dysfunction studied by ^{99m}Tc-DTPA in hypertensives and normotensive controls. *Am J Physiol Imaging* 1986;1:83–90.