ACKNOWLEDGMENTS

The authors thank Mrs. L. C. Hsu for valuable technical support.

This work was supported in part by Medical Research funds (Program 821) of the Veterans Administration.

References

1. Wilcke JR: Idiosyncrasies of drug metabolism in cats. In *Veterinary Clinics of North America: Small Animal Practice*, Vol. 14, No. 6, *Advances in Feline Medicine*, 1984, pp 1345–1354

Marguerite T. Hays
Michael R. Broome
Jane M. Turrel
VA Medical Center
Palo Alto, California
Schools of Medicine and Veterinary Medicine
University of California, Davis
Davis and Sacramento, California

Renal Handling of Technetium-99m DMSA: Further Evidence for Glomerular Filtration and Proximal Tubular Reabsorption

TO THE EDITOR: In their experimental study "Differential Renal Function in Unilateral Renal Injury: Possible Effects of Radiopharmaceutical Choice" (*1*) Drs. Taylor and Lallone refer to our first report on [^{99m}Tc]DMSA in patients with proximal tubulopathy (*2*). The authors state that additional information is needed to determine the mechanism of [^{99m}Tc]DMSA kidney handling. Recently, we found additional evidence that [^{99m}Tc]DMSA, indeed, might be accumulated by glomerular filtration and subsequent tubular reabsorption:

1. Simultaneously measured clearance of iodine-125-(^{125}I) iothalamate and [^{99m}Tc]DMSA shows that the relative [^{99m}Tc]DMSA clearance (expressed as % of the [^{125}I]iothalamate clearance) is 6–13% over a wide range of glomerular filtration rates (GFR) (20–140 ml/min/1.73 m^2). Only in patients with proximal tubular disorders is this relative [^{99m}Tc]DMSA clearance higher and it increases (14–36%) the more the GFR diminishes (*3*). The relation of the filtered load and the urinary excretion of [^{99m}Tc]DMSA can be represented by a straight line, steeper for the patients with tubulopathy than for others, but both lines pass through the origin (*4*).

2. In patients with renal artery stenosis, treatment with captopril can result in lowering of the GFR in the affected kidney to nearly zero; in these cases [^{99m}Tc]DMSA—as well as the [^{99m}Tc]diethylenetriaminepentaacetic acid (*5*)—uptake in that kidney is absent while [^{123}I]hippurate accumulation and excretion still takes place. After withholding captopril, the GFR improves and [^{99m}Tc]DMSA uptake returns (*6*).

3. The plasma protein binding of [^{99m}Tc]DMSA has been considered as an argument against glomerular filtration. On theoretic grounds, it is probable that it is the unbound fraction of [^{99m}Tc]DMSA that is filtered by the glomerulus: after i.v. injection 90% of the tracer is protein bound for some hours while the absolute amount of the tracer in blood is decreasing rather fast ($T_{½}$: 30–40 min). This loss of tracer from the circulation suggests a weak plasma protein binding. Experimental studies to confirm this hypothesis are in progress. These findings point to glomerular filtration and proximal tubular reabsorption of [^{99m}Tc]DMSA. In cases of diminished filtration the kidney uptake is low, even while tubular function is retained (renal artery stenosis and captopril experiment), and in cases of proximal tubular dysfunction urinary loss of the tracer is increased.

References

1. Taylor A, Lallone R: Differential renal function in unilateral renal injury: Possible effects of radiopharmaceutical choice. *J Nucl Med* 26:77–80, 1985
2. van Luijk WHJ, Ensing GJ, Piers DA: Low renal uptake of ^{99m}Tc-DMSA in patients with proximal tubular dysfunction. *Eur J Nucl Med* 8:404–405, 1983
3. van Luijk WHJ, Ensing GJ, Meijer S, et al: Is the relative ^{99m}Tc-DMSA clearance a useful marker of proximal tubular dysfunction? *Eur J Nucl Med* 9:439–442, 1984
4. Piers DA, van Luijk WHJ, Donker AJM, et al: The renal uptake of ^{99m}Tc-DMSA; evidence for glomerular filtration and tubular reabsorption. In *Proceedings 22nd International Annual Meeting, Soc Nucl Med Europe*, Helsinki, Stuttgart-New York, Schattauer Verlag, 1984, pp 427–430
5. Wenting GJ, Tan-Tjiong HL, Derkx FHM, et al: Split renal function after captopril in unilateral renal artery stenosis. *Br Med J* 288:886–890, 1984
6. Kremer Hovinga TK, Beukhof JR, van Luijk WHJ, et al: Reversible diminished renal ^{99m}Tc-DMSA uptake during converting-enzyme inhibition in a patient with renal artery stenosis. *Eur J Nucl Med* 9:144–146, 1984

W.H.J. van Luijk
D.A. Piers
H. Beekhuis
S. Meijer
University Hospital
Groningen, The Netherlands

Failure of a Trial of Oral Phosphate to Enhance Parathyroid Adenoma Detectability on Dual Isotope Scintigraphy

TO THE EDITOR: In a recent publication by Gupta and Belsky concerning the use of oral phosphate to enhance visualization of enlarged parathyroids on imaging (*1*), it was reported that in two of three patients treated with oral phosphate, 1 g/day for 10–21 days, a repeat parathyroid scan showed increased detectability of a previously localized adenoma. After oral phosphate therapy in two patients, serum parathyroid hormone (PTH) increased from baseline while serum calcium decreased; in the third patient, no changes in laboratory data occurred.

Gimlette and Taylor related the serum PTH levels to the detectability of the adenomas, resulting in a positive correlation between the two if the PTH levels were greater than 600 pg/l (*2*). Therefore, it seems that detectability of parathyroid adenomas may be improved by administering an oral phosphate solution which will bring about a decrease in serum calcium levels and an increase in PTH levels (*1,2*).

To validate this theory, we studied six patients who clini-

cally and biochemically had primary hyperparathyroidism. All six patients had initial negative parathyroid images with technetium-99m/thallium-201 dual isotope scintigraphy using the technique described by Gordon and Carr (*3*).

A blood sample was drawn for serum calcium, serum phosphate, and PTH levels. Our measurement of PTH was by radioimmunoassay using the PTH mid-molecular portion. A normal range was 0–85 pm/l with a normal serum calcium. The patients were then given Fleets Phospho-Soda, 1/2 teaspoon three times daily for 7 days, which provided ~1 g/day of phosphorous. Upon return to our laboratory, a second blood sample was drawn for the above parameters, and the patients were re-imaged.

The results revealed that in all six patients serum calcium and phosphate levels decreased while the PTH level slightly increased in two, decreased in three, and was not available in one patient. Only in one patient was the second image read as being positive, and in this patient the PTH was not available. In this patient, the presence or absence of an abnormality on the first image reading was debated, but officially it was read as negative. To date, none of these six patients has undergone surgical exploration to definitively identify the presence or absence of parathyroid disease.

An underlying purpose in our using phosphate intervention was to evaluate its possible use as a routine premedication for the dual isotope scintigraphy. However, since the results of the images were not significantly altered, we do not feel oral phosphate therapy to be beneficial; nor should it be used routinely.

References

1. Gupta S, Belsky J: Use of oral phosphate to enhance visualization of enlarged parathyroids on scanning (lett). *J Nucl Med* 26:100–101, 1985
2. Gimlette TMD, Taylor WH: Localization of enlarged parathyroid glands by thallium-201 and technetium-99m subtraction imaging, gland mass and parathormone levels in primary hyperparathyroidism. *Clin Nucl Med* 10:235–239, 1985
3. Gordon L, Carr D: Preoperative localization of parathyroid adenomas using thallium-201 technetium-99m subtraction scintigraphy. *So Med J*: in press

Donna S. Carr
Betty S. Roof
James F. Cooper
Leonie Gordon
Departments of Clinical & Institutional Pharmacy
Endocrinology and Radiology
Medical University of South Carolina
Charleston, South Carolina

REPLY: We read with interest the letter of Carr et al. about their experience with the use of oral phosphate to enhance parathyroid adenoma detectability on dual isotope scintigraphy. Limitation of resolution is a major problem with scanning parathyroid adenomas, with 0.250 g being the lower limit in our experience (*1*). It is possible that small adenomas in the cases of Carr et al. may have been below the resolution limits. Of course, one would also have to take into account the possibility of hypercalcemia being due to causes other than primary hyperparathyroidism in their patients, especially since they all had negative initial images.

The dose and duration of phosphate therapy is another important factor which may influence the results. We found in two patients the use of oral phosphate, 1 g/day for three weeks resulted in elevation of PTH with enhancement of already visualized adenomas. In one patient however, oral phosphate 1 g/day for only 10 days did not influence the calcium, PTH, or the scan. The use of phosphate for only 7 days in their cases was therefore probably not sufficient as was seen in their results where only two out of six patients had slight increase in PTH level.

In conclusion, therefore, the subjects studied by Carr et al. were not strictly comparable to our cases because of having negative initial images and a much shorter course of phosphate administration. Our cases with enhanced images also had definite PTH elevation after phosphate administration.

We agree with Carr et al. that routine use of phosphate is not indicated at the present time but also believe that this maneuver does provide a way to enhance imaging in appropriate patients where initial images may have been equivocal. One might be able to judge whether re-imaging is worthwhile following phosphate therapy by assessing PTH level in comparison with a baseline study.

References

1. Gupta SM, Belsky JL, Spencer RP, et al: Parathyroid adenomas and hyperplasia. Dual radionuclide scintigraphy and bone densitometry studies. *Clin Nucl Med* 10:243–247, 1985

Shiv M. Gupta
Joseph L. Belsky
Danbury Hospital
Danbury, Connecticut

Correction: Cardiovascular Nuclear Medicine-Training for the Future

In an Editorial appearing in *J Nucl Med* 27:1642–1643, 1986, Reference *1* should read as follows:

1. McPhee SJ, Garnick DW: Imaging the heart:Cardiac scintigraphy and echocardiography in U.S. hospitals. *J Nucl Med* 27:1635–1641, 1986