

determination after T<sub>3</sub> withdrawal or thyroidectomy in the therapy of thyroid carcinoma. *J Nucl Med* 20:928-932, 1979

- HAMBURGER JI: Diuretic augmentation of I-131 uptake in inoperable thyroid cancer. *N Engl J Med* 280:1091, 1969

## Reply

We have found no data in the literature to support Dr. Hamburger's assumption that in metastases radioiodine uptake will continue to increase with prolonged exposure to high TSH levels. Although this is a theoretical possibility, there are practical reasons for minimizing the duration of hypothyroidism. Protracted hypothyroidism is poorly tolerated by patients, it may have medical complications and it may be associated with tumor growth. Accordingly, we have chosen to administer radioiodine at the time of maximal pituitary TSH secretion and to keep the period of hypothyroidism as short as possible.

After thyroidectomy residual uptake of radioiodine in the thyroid bed is usually associated with residual normal, functioning thyroid tissue. Such uptake can often be ablated with a single dose of I-131. Successful ablation of thyroid bed uptake should not be confused, however, with eradication of uptake in functioning metastases; the latter often requires repeated treatment with I-131.

Low iodine diets may augment tumor uptake of I-131 by decreasing the amount of stable, carrier iodine in the body; such diets require rigid patient compliance in view of the widespread introduction of iodine into food and food additives. The use of ethacrynic acid to deplete body iodine as advocated by Hamburger (1), however, may cause serious side effects. Nemec et al. reported clinical intolerance to ethacrynic acid pretreatment such as drowsiness, muscular weakness, arterial hypotension, and manifestations of previously latent tetany (2). When ethacrynic acid is stopped renal iodide clearance falls sharply, which results in increased body retention of I-131 and increased whole body radiation; this effect is independent of I-131 uptake in the tumor. As Sisson has observed, a similar effect of increased tumor and whole body radiation can be achieved simply by increasing the dose of I-131 (3).

DOROTHEA HELLMAN  
JAMES WOOLFENDEN  
SCHUYLER HILTS  
Pima Professional Plaza  
Tucson, Arizona

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## Glucuheptonate Kidney Studies

The comparison of Tc-99m glucuheptonate renal imaging with the i.v. urogram for the detection of mass lesions, reported by Leonard et al. (1), was impressive (accuracy 85% against 71%).

Since their findings confirm my impression and that of many other clinical groups using Tc-99m glucuheptonate since 1974, it is surprising that no previous report on glucuheptonate imaging has appeared in the medical literature. (Glucuheptonate has been reported to be equivalent to iodohippurate for the evaluation of renal function (2).) This report (1) with its excellent results is, therefore, particularly welcome, since one is reluctant to recommend a new procedure over a well-established test solely on the basis of anecdotal experience. The report was incomplete however, and the results as reported were almost certainly less favorable to glucuheptonate than actual clinical experience would indicate, considering that six of 47 cases were excluded because urograms were considered inadequate for interpretation.

It would be of interest to know what occurred in the clinical setting, in addition to the reported results of comparative evaluation later "reviewed independently by two observers without benefit of clinical history." How were the 47 radiographic and radionuclide studies initially reported, and how did this affect clinical management? Were six to eight urograms initially considered inadequate and a radionuclide study therefore recommended? If the initial diagnostic study, whether radiographic or radioactive, were considered adequate, why was the other study done? Unless this was a prospective clinical research project, the second study should have been considered redundant, before knowing the results of this comparison report. What were the clinical indications for these studies and in the other patients who had glucuheptonate renal imaging alone? I doubt that a scan would have been preferred initially over i.v. urography (IVU) for suspicion of neoplasm. Heretofore, the most common indication for radionuclide studies has been inability to perform IVU because of either allergy to iodine or impaired kidney function; less commonly to determine the cause of impaired function, or of hypertension, of the vascularity of a lesion demonstrated by IVU; or to evaluate other aspects of function, such as obstructive uropathy.

The authors (1) state that the radionuclide flow study was not found "to be reliably helpful in evaluating the vascularity of mass lesions." They must mean that a cyst may mimic a mass lesion, as has been reported previously. How accurate was the flow study in differentiating cysts from mass lesions? I have found the flow study extremely important in this regard; including one patient with hypertension shown to have a highly vascular kidney lesion, said to be a cyst by ultrasound but proved to be hypernephroma. (Ultrasound was redundant as well as wrong in that case, since biopsy is indicated unless a lesion appears avascular as well as cystic by ultrasound.)

The authors (1) suggest the possibility of missing extrarenal disease if only radionuclide studies are performed, but add that no significant extrarenal disease was detected by IVU in their cases. In how many of their patients was significant extrarenal disease detected in radionuclide studies? In one published report, clinically unsuspected significant findings were discovered in 22% of patients by radionuclide studies (3). I continue to be amazed at the high incidence of significant incidental findings in Tc-99m kidney studies, visualized primarily in a vascular flow study. Two of the most striking examples have been published (4,5). I have also found aortic aneurysm and pseudo-aneurysm; extrarenal neoplasm, inflammatory disease, and hematoma; and occlusive peripheral arterial disease. Conversely, when the vascular flow study has been done to evaluate arterial disease, kidney abnormalities are often discovered.

I am sure that Dr. Leonard's article will encourage more extensive use of this important diagnostic modality, and I hope other groups will evaluate their experience with Tc-99m glucuheptonate kidney studies for publication.

RALPH S. WOLFSTEIN  
Century City Hospital  
Los Angeles, California

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### Renal Cortical Imaging and the Detection of Renal Mass Lesions

Leonard et al. reported the usefulness of the Tc-99m glucoheptonate renal scintigram in detecting renal cortical mass lesions in comparison with the radiographic modalities, such as the excretory urography and renal angiography (1). Although in their discussion these authors described the usefulness of the radionuclide dynamic flow study to evaluate the vascularity of cortical mass lesions, further application of renal cortical scintigraphy should aid in the differentiation of renal space-occupying or mass lesions. We attempted to differentiate cortical vascular lesions from cortical cysts by combining early dynamic and late static images using Tc-99m dimercaptosuccinic acid (DMSA), instead of Tc-99m glucoheptonate (2).

For the past several years, Tc-99m DMSA has been used more frequently in Japan as a renal imaging agent. Since this radionuclide accumulates preferentially in the renal cortex, the late image provides a distinct static cortical image, whereas the early image shows dynamic flow through the vascular pool in the renal cortex (3,4). After 2 mCi of Tc-99m DMSA were administered intravenously, early images were obtained after 20 to 50 sec and the late images after 2-3 hr. As is shown in Fig. 1, in cases of renal cortical malignancy, such as renal-cell carcinoma, local Tc-99m DMSA uptake can be detected on the early image (left-hand arrow) and, because of the nonfunctioning cortical mass, an area of decreased activity should appear in the same area on the late image (right-hand arrow).

In the case of renal cystic lesions, the area of decreased activity was revealed in both early and late images with almost 100% di-



**FIG. 1.** Renal-cell carcinoma in upper lateral portion of left kidney. Increased activity at site of tumor (white arrow) is seen in early image, and area of decreased activity in same location (dark arrow) in late image.

agnostic accuracy. In cases of renal-cell carcinoma and angiomyolipoma, Tc-99m DMSA uptake was seen in the early image and the area of decreased activity was observed in the late image, indicating the diseased region. However, Tc-99m DMSA uptake was not seen in the early image in cases where a renal-cell carcinoma had advanced to the stage of necrosis. Occasionally when a highly vascular renal tumor had extended into the perinephric tissues, the tumor area could be overestimated on the early image.

It is almost impossible to diagnose renal-cell carcinoma using the radionuclide image alone. However, Tc-99m DMSA renal studies, with both early and late imaging, have proven to be a useful, noninvasive adjunct in the detection of malignant cortical lesions.

JUICHI KAWAMURA  
Kyoto University Hospital  
Kyoto, Japan

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### Reply

Dr. Wolfstein is correct that our clinical experience with glucoheptonate is better than the reported statistics. We find ourselves in the camp claiming that all nuclear medicine studies can best be interpreted with full knowledge of the clinical information and other ancillary studies. To avoid the biases inherent in that view, however, our study was designed as a double-blind comparison. We hope our results will encourage the use of radionuclide scintigraphic procedures as a primary method for the evaluation of suspected renal mass lesions rather than being considered a substitute for the intravenous urography (IVU).

The majority of our reported patients were managed on the basis of the IVU report. Glucoheptonate was still investigational during the time of the study and it is only recently that the primary physicians have had confidence in the results. The six urograms that were not included were judged inadequate during the double-blind review. Although the radionuclide studies in these patients were all valid and useful, we decided not to include these patients because we were comparing results for adequate IVU and glucoheptonate scintigraphy. Including these patients would have improved the statistics but could be criticized since it would have been argued that the IVU should have been repeated. Including these patients would have decreased the IVU accuracy to approximately 70% without materially changing the glucoheptonate results. We do not have data on how many of the radionuclide studies were obtained because the primary physician felt the IVU was inadequate, rather than receiving the study as part of the investigational protocol.

While we appreciate Dr. Wolfstein's and Dr. Kawamura's comments on renal flow studies, we have found routine flow studies