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**LABORATORY OF NUCLEAR MEDICINE
AND
RADIATION BIOLOGY**

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MASTER

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RADIONUCLIDE EVALUATION OF
RENAL TRANSPLANT STATUS

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INTRODUCTION

Management of the renal transplant recipient is aided by successful prediction of early rejection, and/or diagnosis of other causes of dysfunction. Conventional methods of evaluation such as clinical signs and symptoms, laboratory values, and fluid balance data often lag behind acute alterations in transplant function status. Previous studies have compared the usefulness of this data as well as blood and urine histamine levels with radionuclide studies such as the renogram, the hippurate clearance index, the radionuclide angiogram and quantitated sequential renal scintiphotos [5]. Of these methods the bladder/kidney ratio derived from quantitated scintiphotos was found to be the single most useful indicator of transplant function, and the most sensitive and reliable predictor of rejection [6]. This paper summarizes 5 years of experience and presents a practical protocol for radionuclide evaluation of transplant status, emphasizing the prediction of acute rejection and avoidance of certain pitfalls associated with the recommended procedures.

METHOD

Radionuclide studies were performed on a frequent basis on human renal homotransplant recipients for at least two weeks postoperatively. Serial scintiphotos were obtained with a Picker Dynacamera 2 with the patient in a supine position following bolus intravenous administration of 300 μ Ci of ^{131}I -hippurate. Renogram and cystogram curves were then generated from magnetic tape recorded data. Simultaneously the blood disappearance rate

of the injected dose of hippurate was monitored with an external detector placed over the anterior chest. When there was little significant renal uptake of ^{131}I -hippurate, an intravenous radio-pertechetate angiogram was performed. The following indices were calculated and tabulated: renogram downslope indices [9, 11, 12]; hippurate blood clearance index [8, 1, 2]; bladder/kidney ratio at 20 minutes post-injection [4]; minimum bladder entry time [3]; and kidney/background ration at 20 minutes post-injection [7]. Each of these radionuclide indices were correlated with the patient's clinical course, fluid balance data and serum chemistries.

RESULTS AND DISCUSSION

During a five year period 580 examinations were performed on 72 post-renal homotransplant recipients during the first 14 post-operative days. Results were analyzed as described under Method. In approximately 1/3 of these patients a clinically recognized rejection crisis, ranging from mild to severe, occurred during this period of time.

The calculation of renogram indices was discontinued about half way through the study as being significantly less sensitive and less reliable than the remaining parameters to be discussed.

The hippurate blood clearance index, although generally sensitive, was found to show transient paradoxical improvements just preceding rejection crisis about 50 per cent of the time. This phenomenon is apparently related to an outpouring of histamine, which may occur in the days prior to clinical rejection [10] and cause an increase in extravascular extravasation of hippurate.

This index was found useful and is determined daily regardless of the general level of transplant function.

The bladder/kidney ratio, derived from quantitated scintiphotos at 20 minutes post-injection, not only proved to be the most sensitive indicator of transplant function, but in over 80% of all cases of early rejection there was a significant drop from 1 to 3 days before clinical rejection, as illustrated by figure 1. In acute rejection there was usually a temporary increase in the blood clearance index in association with the fall in bladder/kidney ratio. In delayed hyperacute rejection, associated with presensitization, there were simultaneous marked drops in the blood clearance index and the bladder/kidney ratio. In 20% of the cases in which there was no definite clinical evidence of a rejection crisis, there were transient false positive reductions in the bladder/kidney ratio occurring at the end of post-transplant diuresis. In most of these cases the simultaneously performed blood clearance index remained stable. In a few instances failure to clamp an indwelling bladder catheter caused completely inaccurate bladder/kidney ratios and also made determination of bladder entry time more difficult. Another cause of falsely depressed bladder/kidney ratio was pooling of urine in the renal pelvis or partial obstruction at the uretero-vesical junction. These last two causes were very infrequent in our series and readily detected by inspection of sequential scintiphotos. This index was most useful when transplant function was good as judged by good renal uptake with a fair to good bladder accumulation at 20 minutes post-injection (bladder/kidney ratio greater than 1.0).

At such times transplant status was best followed by daily bladder/kidney ratios. When the bladder/kidney ratio was less than 1.0 it was no longer found to be the most useful or accurate index and in some cases was actually misleading. Results with more useful indices when function is nil, poor, or only fair will be reported in succeeding paragraphs.

When function was nil as judged by no visualized uptake of hippurate at 20 minutes post-injection, an intravenous radiopertechetate angiogram aided in differentiating tubular necrosis from arterial blockade or severe hyperacute rejection.

When function was poor as judged by presence of some renal hippurate uptake but absence of activity in the bladder, the kidney/background ratio at 20 minutes post-injection was the most useful index for comparison with subsequent studies. Figure 2 illustrates a case in which improving kidney/background ratios predict eventual good function in a patient recovering from some tubular dysfunction. We have found the comparison of daily kidney/background ratios more useful in such cases than pertechetate "flow" studies. A pre-injection scintiphoto should be performed after the first study; and residual counts, if any, from previous examinations should be subtracted from post-injection values to obtain an accurate ratio.

When function was fair as judged by poor to fair bladder accumulation 20 minutes post-injection (bladder/kidney ratio less than 1.0) daily estimations of minimum bladder entry time determined by inspection of sequential renal scintiphotos provided the best means of monitoring progress or detecting setbacks. Figure 3

illustrates a case in which improving bladder entry times predict eventual good function.

The level of transplant function at 24 hours postoperation according to the above definitions was as follows for our series: nil, 5%; poor, 32%; fair, 23%; good, 40%.

Since experience to date has led us to feel that in the early postoperative period the more frequently radionuclide studies are performed upon a given transplant recipient, the more accurately rejection could be predicted, our present protocol is to begin hippurate studies at 24 hour post-transplant and continue them daily. The index used for evaluation and prognostication at any given point in time is selected according to the general level of function as discussed above. Radionuclide procedures are now discontinued after the fourteenth day as after that time they seem to have no clear advantage over conventional laboratory methods for the assessment of transplant function.

CONCLUSIONS

Quantitated sequential renal scintiphotos performed with ^{131}I -hippurate were more sensitive than serum chemistries and clinical signs as indicators of renal transplant status, and were often successful in predicting acute rejection crises. The most useful indices depending on the general post-transplant level of function were the kidney/background ratio at 20 minutes post-injection, the minimum bladder entry time post-injection, and the bladder/kidney ratio. In the few cases where it was necessary to differentiate tubular necrosis from hyperacute rejection, intravenous radionuclide angiography was helpful. Successful

prediction of rejection depended on the performance of daily studies and careful following of changes in the recommended indices.. False positive rejection predictions were minimized by careful correlation with the patient's fluid balance information and hippurate blood clearance index.

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LEGENDS

Figure 1. Kidney-bladder scintiphotos 20 minutes post-injection of ^{131}I -hippurate in a renal transplant recipient before and during a rejection crisis which began on the 7th post-operative day. Note that while the bladder/kidney ratio predicts rejection both blood clearance index and serum creatinine levels are misleading.

- (A) "Good" function 4 days post-transplant (bladder/kidney ratio = 4.1; blood clearance index = 287; serum creatinine = 1.5 mg/100 cm³).
- (B) 6 days post-transplant showing prolonged renal retention of ^{131}I -hippurate before onset of clinical rejection (bladder/kidney ratio = 1.6; blood clearance index = 307; serum creatinine = 1.2 mg/100 cm³).
- (C) 9 days post-transplant showing slow uptake of hippurate by the transplant and lack of significant activity in the bladder by 20 minutes post-injection (bladder/kidney ratio = 0.5; blood clearance index = 105; serum creatinine = 8.2 mg/100 cm³).

Figure 2. Kidney-bladder scintiphotos 20 minutes post-injection of ^{131}I -hippurate in a renal transplant recipient illustrating use of the kidney/background ratio when an insignificant quantity of activity has reached the bladder. Note that use of the bladder/kidney ratio or blood clearance index for the first two examinations would have been misleading.

- (A) "Poor" function one day post-transplant (kidney/

- background ratio = 2.0; bladder/kidney ratio = 0.5; blood clearance index = 162).
- (B) Two days post-transplant (kidney/background ratio = 3.0; bladder/kidney ratio = 0.33; blood clearance index = 122).
- (C) Ten days post-transplant showing "good" transplant function (bladder/kidney ratio = 1.8; hippurate blood clearance index = 267).

Figure 3. Twenty minute "area of interest" camera renograms and cystograms with ^{131}I -hippurate showing usefulness of bladder entry time (indicated by white arrow over the cystogram) as a prognosticator of recovery from a rejection crisis which occurred 11 days post-transplant. Note that the bladder/kidney ratio fails to indicate improving condition of the transplant for the first two studies. Bladder entry time is most easily determined by inspection of serial scintiphotos although it may also be determined by noting the point at which the cystogram begins rising as illustrated.

- (A) "Fair" function twelve days post-transplant (bladder entry time = 14 minutes; bladder/kidney ratio = 0.4; blood clearance index = 174).
- (B) Twenty days post-transplant (bladder entry time = 8 minutes; bladder/kidney ratio = 0.4; blood clearance index = 198).
- (C) Twenty-seven days post-transplant (bladder entry time = 4 minutes; bladder/kidney ratio = 1.8; blood clearance index = 248).