TEACHING EDITORIAL

In Vivo Function Tests in Nuclear Nephrology:
An Improved Modification of the
"Old Probe" Techniques?

Recent availability of technetium-99m-labeled renal tracers and the ready availability of computer processing have rekindled interest in the in vivo function studies (1–4) that had been relegated to a secondary role during the flourishing era of organ-imaging procedures. Previously established radionuclide methods for the assessment of renal function have been generally difficult to standardize, require critical attention, suffered from procedural and analytical complexity, and were hampered by radioagents with suboptimal physical and biologic properties (5–7). Except for the I-131 hippuran renogram, in vivo renal function studies acquired limited acceptance as routine diagnostic procedures in the clinical nuclear medicine laboratory.

Standard biochemical plasma and serum renal function profiles lack specificity and sensitivity. Normal laboratory values that reflect apparently normal renal function can be observed when more than half of the functional parenchyma has been destroyed (7–9). Because of these limitations, renal physiologists have recommended the measurement of glomerular filtration rates (GFR) by inulin clearance and the assessment of effective renal plasma flow (ERPF) by para-aminohippurate (PAH) dilution techniques for precise assessment of renal function. Unfortunately these procedures are relatively complicated and cumbersome, and require continuous hour-long infusion, urinary catheterization and frequent blood sampling. This diagnostic approach is even less desirable when the function of each kidney needs to be assessed and ureteral catheterization is required. Such invasive, time-consuming techniques cannot be performed frequently and are not suitable for routine clinical use. Despite the rather poor reproducibility and high interlaboratory variation, the creatinine clearance has generally replaced these more complicated and elaborate clearance tests. The measurement of creatinine clearance requires 24-hr urine collection to diminish collection and bladder-emptying errors. The difficulty with ensuring adequate 24-hr urine is a well-known clinical problem that has been frequently documented. Furthermore, creatinine clearance often significantly overestimates glomerular filtration rate in nephrotic syndrome and terminal renal failure (9). Although the traditional radionuclide clearance techniques utilizing I-131 iohippurate and sodium diatrizoate were originally designed on the same theoretical basis as the chemical techniques and did obviate the need for continuous infusion (5), they did not provide significant simplification.

A relatively simple technique for the evaluation of in vivo renal function—one that is rapid, reproducible, easily standardized, and allows serial evaluation of global and individual unilateral renal function—is needed for routine clinical use. Such a test must be reliable for the identification of normal and slightly-to-moderately decreased renal function, since biochemical screening procedures may be misleading during early periods of evolution of renal disease when recognition of renal dysfunction might allow therapeutic modification. In addition, an in vivo renal function test should provide measurement of global renal function, split function, and regional function within each kidney.

The preliminary report by Andrew Taylor and Lee B. Talner, “Relative Renal Accumulation of Technetium-99m Penicillamine as an Index of Differential Renal Function” (10), which appears in this issue of the Journal, may provide a radionuclide renal function test that meets some of the criteria detailed above.

Their data, although limited by the number of patients studied, indicate comparable split-function results using technetium-99m penicillamine and creatinine clearance. Their computer-assisted data acquisition and analysis of area-of-interest histogram are technically reproducible. The basic concept and technique presented by Taylor and associates are similar to those originally described by Reba et al. (11). By means of a dual-probe system and a strip-chart recorder, Reba measured the renal uptake of chloromerodrin to screen hypertensive patients for the presence of unilateral renal artery stenosis.
They hoped that the chloromerodrin kidney uptake test would be an indicator of renal blood flow, whereas the hippuran renogram would be an indicator of cortical tubular function. It soon became obvious, however, that abnormal unilateral patterns with either agent were essentially nonspecific and were associated with renal artery stenosis or primary parenchymal disease (6, 7). Cortical tubular function is dependent in part on cortical renal blood flow and glomerular capillary integrity; therefore, agents such as chloromerodrin, penicillamine, diethylysuccinic acid, and others that localize in the proximal and distal convoluted tubules should reflect the function status of all the cortical segments of the nephron, linked together as a functional unit by their characteristic pattern of vascular supply. We can further hypothesize that under proper procedural standardization essentially identical results may be obtained from renal radiopharmaceuticals specifically interacting with renal cortical blood flow, glomerular filtration, or cortical tubular cell function. For more than a decade Claud Raynaud and his colleagues (12) evaluated the significance of mercury-197 chloride uptake against a dose phantom and found good correlation between mercury uptake and the standard renal clearance tests of inulin, PAH, and creatinine. The relative symmetry of mercury chloride uptake in patients with normal renal function suggested that asymmetry should indicate the most sensitive index of renal disease and permit detection before total uptake diminishes and function becomes subnormal. Raynaud's technique has proved invaluable for the assessment of surgical and medical management of bilateral and unilateral renal pathology.

The procedure recommended by Taylor et al. is certainly intriguing because of its simplicity and its apparently good correlation with creatinine clearance. This relative simplicity in obtaining results, not only for patients but also for the examiner, could make this type of in vivo renal function test using a technetium-99m-tagged renal agent an acceptable routine procedure that we should continue to investigate.

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REFERENCES