

External Monitoring of Kidney Transplant Function Using Tc-99m(Sn)DTPA

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The purpose of this study was to evaluate the use of an external counting technique to provide daily monitoring of kidney transplant function by measuring the renal clearance of Tc-99m(Sn)DTPA. During the first few weeks following transplant, 15 patients had their renal clearance of Tc-99m DTPA measured daily over periods of 5–24 hr. Clearance rates were compared with daily plasma creatinine levels, and the effects of diurnal variation, drug treatment, and physical activity noted. The results show that any significant fall in clearance rate of chelate, indicating a rejection episode, preceded a rise in plasma creatinine levels by at least 24 hr. One episode of transplant failure presented as a sudden deterioration in clearance rate of chelate; in the others the change was more gradual but was still apparent within hours. It is considered that this noninvasive, low-dose, easy-to-perform technique is of considerable value in extended daily monitoring of renal function and is superior to standard daily or twice-weekly renography for the early detection of transplant rejection.

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Labeled DTPA and EDTA complexes have been used to measure renal glomerular function with reasonable success and accuracy for the past decade (1–3). Although Tc-99m(Sn)DTPA (Tc-99m DTPA) was initially inferior to Cr-51 EDTA in the measurement of the GFR, recently introduced kits (4) give practically identical clearance rates and have the added advantage of being ideal for gamma-camera measurements due to the 140-keV gamma emission from Tc-99m. To obviate the need to obtain serial blood and urine samples, external radionuclide counting methods have been developed using these labeled chelates, which give a simple accurate, noninvasive technique for the measurement of renal glomerular function (5,6).

Standard probe renography and computerized dynamic renal emission studies have been performed ex-

tensively to study diseased renal function and morphology, using either orthoiodohippurate (I-131 or I-123) or Tc-99m DTPA, but each study period is short, usually 15–20 min (7). In the case of renal transplant patients, renography is routinely performed daily or twice weekly, thus any sudden change in kidney function, (e.g., an acute rejection episode) can remain undetected for as long as 24 hr—the time it takes for significant changes in blood chemistry to develop—or until renography is next performed. Thus valuable time can be lost before instituting appropriate therapy.

TABLE 1. PERCENT PROTEIN BINDING OF Tc-99m DTPA

Batch	1st. dose	Last dose	Mean
1	3.2	3.6	3.4
2	3.0	3.4	3.2
3	2.8	3.6	3.2

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TABLE 2.

Study no.	Rejection episode	Rejection detected by		
		Rise in $t_{1/2}$ biol.	Rise in plasma creatinine	Cause of rejection, and biopsy findings
1	First	Day 10	Day 12	Wound abscess, explored surgically
2	First	Day 14	Day 16	19th day mild cellular rejection
3	First	Day 10	Day 11	11th day exploration, urine leak
4	First	Day 9	Day 10	11th day, cellular rejection
4	Second	Day 21	Day 25	27th day, moderate cellular rejection
5	First	Day 8	Day 9	11th day, severe vascular rejection, graft nephrectomy
6	First	Day 10	Day 12	13th day, biopsy inconclusive
	Third	Day 25	Day 26	31st day, vascular rejection
7	First	Day 10	Day 11	12th day, renal infarct
8	First	Day 13	Day 15	19th day, vascular rejection
9	First	Day 5	Day 7	8th day, vascular rejection
10	First	Day 9	Day 11	12th day, wound abscess (no biopsy)
11	First	Day 7	Day 9	12th day, vascular rejection, graft nephrectomy
12	None	—	—	
13	None	—	—	
14	None	—	—	
15	No significant function			Graft nephrectomy

Choice of external counting systems lies between a relatively inexpensive, shielded, sodium iodide detector, which has the disadvantage of being rather bulky, and the lightweight but expensive solid-state detectors, e.g., cadmium telluride, with accompanying data-storage and processing ancillaries. The disadvantage of the lightweight solid-state systems, however, is their depth dependency, and appropriate safeguards and corrections must be made if such a system is used.

Although we have used both types of detector suc-

cessfully, this paper presents the results of a study to evaluate the feasibility of using a simple NaI(Tl) detector and an external arm-counting technique to measure continuously, or at least over a period of 5 hr daily, the clearance of Tc-99m DTPA in renal allotransplant patients.

MATERIALS AND METHODS

Fifteen patients who had received renal allografts were studied from the day following the transplant operation

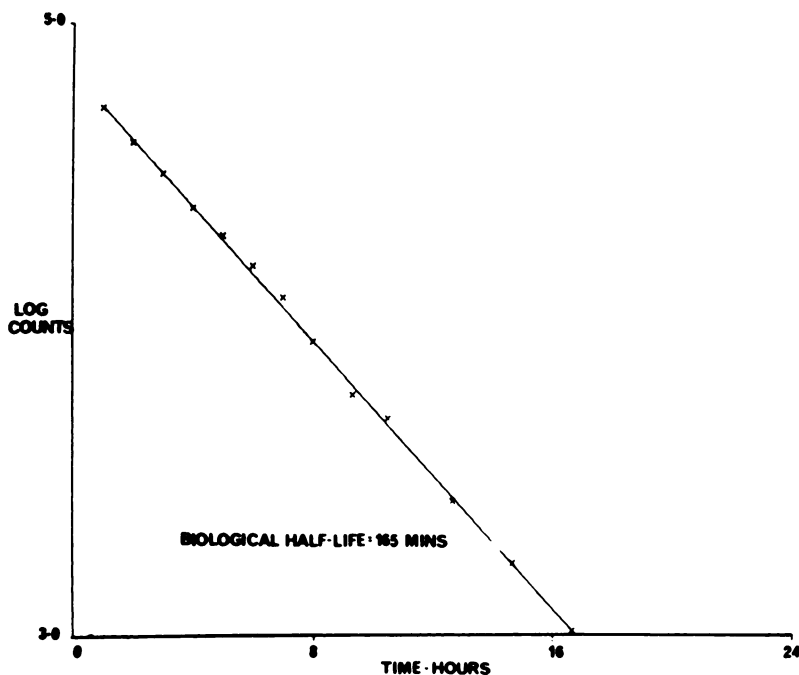


FIG. 1. Plot of 24-hr arm count, corrected for decay and protein binding, on patient with normally functioning transplant.

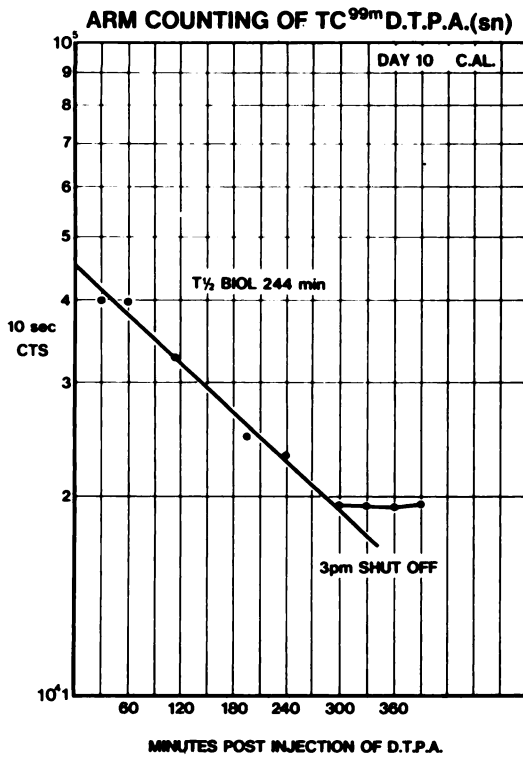


FIG. 2. Rupture of ureteric anastomosis, with sudden cessation of glomerular function.

until they left hospital or the transplant was irreversibly rejected. For the first 9 days following the transplant all patients in this unit receive routine steroid pulsing.

At the beginning of each study, the patient was injected intravenously with 0.5 mCi of freshly prepared lyophilized Tc-99m DTPA* and, where possible, had 1000-sec computerized scintigraphic renography per-

formed in order to assess original renal morphology and function. Subsequently they had their progress monitored by external forearm counting using a 2-in. NaI(Tl) detector with a sleeve collimator, linked to a timer/scaler. Counts were collected for 10 sec, repeated twice and averaged, every 15-30 min, (or as daily patient management allowed) corrected for background, decay, and the percentage of protein binding (δ), and plotted on semi-log paper. Reproducibility measurements for the arm-counting device, using both a cobalt source and the patient's forearm, gave between-count variations of less than 1%. Studies were performed for at least 5 hr, and in two cases up to 24 hr. The number of points plotted ranged from 20-50. Renal clearance of Tc-99m DTPA was measured in terms of the biological half-life of the chelate ($t_{1/2}$ biol.) (3), expressed in minutes, and the exponential plotted for best fit by eye, then checked by least-squares fit on a minicomputer.

Noncomplexed Tc-99m and protein-bound activity occurring in vivo was estimated for the first and last dose obtained from each batch of Tc-99m with a Sephadex G-25 medium-gel chromatograph with a blue dextran marker. The column was then longitudinally scanned with a 2-in. NaI(Tl) crystal and a 1-mm slit collimator. Protein binding was found to be between 3-4%, and noncomplexed Tc-99m was less than 3% (see Table 1). Protein binding of 3-4% may appear unacceptably greater than the 0.4-1.8% found for several Tc-99m DTPA compounds recently evaluated (4,9) but in their studies the protein binding was estimated in vitro in incubated blood, which may well account for the difference. Detection of rejection episodes was confirmed by biopsy in ten out of the 13 studied, and in the remaining three by surgical exploration (see Table 2).

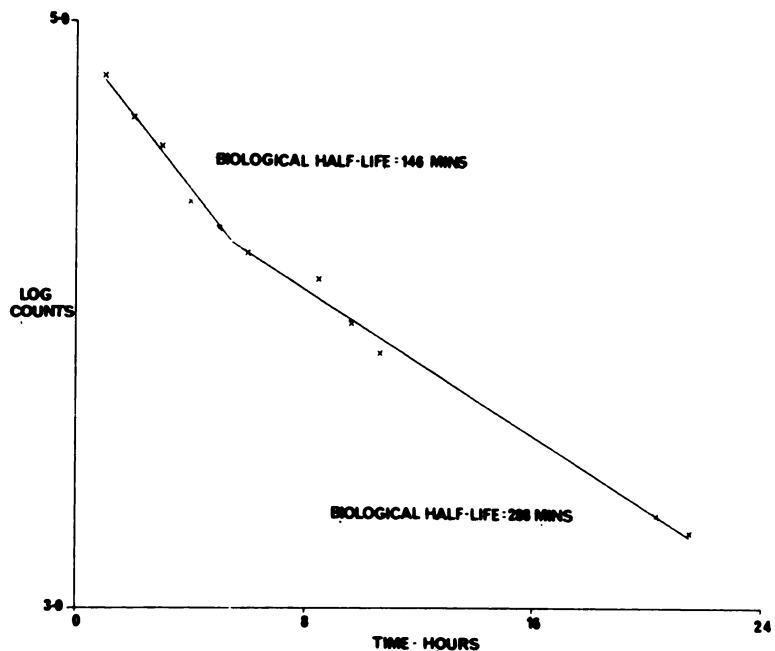


FIG. 3. Rejection episode, with deterioration in renal function over several hours.

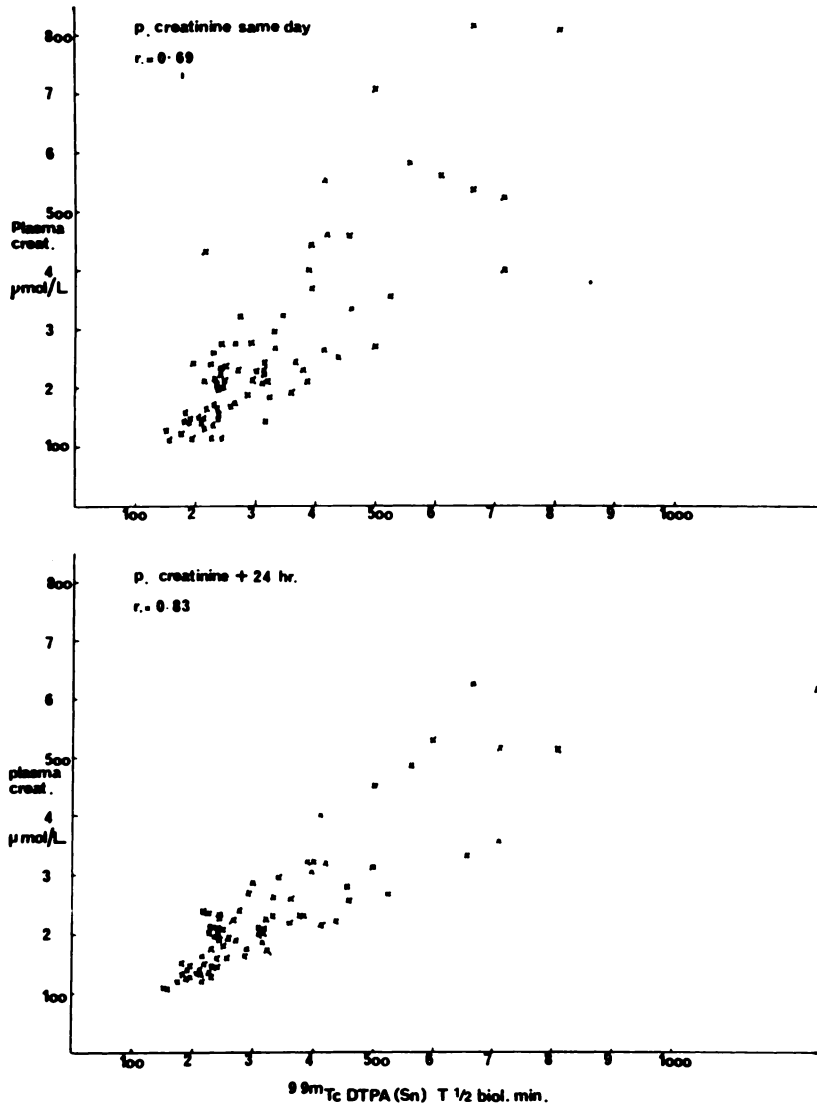


FIG. 4. Correlation between Tc-99m(Sn)DTPA clearance values ($t_{1/2}$) and plasma creatinine levels, as measured on the same day (above) and 24 hr later (below).

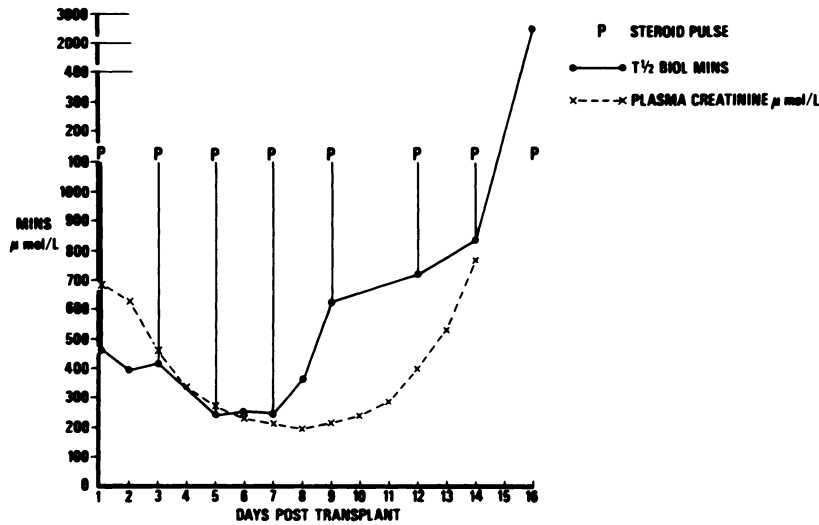


FIG. 5. Comparison between renal clearance of Tc-99m(Sn)DTPA and plasma creatinine levels in patients exhibiting irreversible rejection episode.

RESULTS

Figure 1 shows an example of a plotted 24-hr arm count, corrected for background, decay, and protein binding, on a patient where the transplant was functioning well.

From the results in Table 2 it is apparent that of the 15 allotransplants studied, three had no rejection episodes over the period of the study. In the remaining 12 patients, 12 rejection episodes occurred of which four were irreversible, resulting in death or removal of the kidney. In one patient, rupture of the ureteric anastomosis occurred, with sudden cessation of glomerular function (Fig. 2). Of the eight rejection episodes with recovery after treatment, deterioration of glomerular function was exhibited over a period of hours (Fig. 3).

When the clearance of Tc-99m DTPA was compared with daily plasma creatinine levels in the patients exhibiting rejection episodes, it became obvious that a closer relationship existed between Tc-99m DTPA clearance rates and the plasma creatinine levels occurring 24 hr later, rather than those obtained on the same day. (Correlation coefficients: same day, $r = 0.69$; for 24 hr, $r = 0.83$; see Fig. 4.) Additional evidence that the change in tracer clearance showed better correlation with plasma creatinine levels 24 hr later, and paralleled a deterioration in kidney function, is provided by the fact that same-day plasma creatinine levels were significantly less than those found 24 hr later ($p < 0.005$) and 48 hr later ($p < 0.001$). For patients exhibiting rejection episodes, Figs. 5 and 6 show a comparison between renal tracer clearance and plasma creatinine levels over 16 days. A similar comparison in a patient without any evidence of rejection is shown in Fig. 7.

DISCUSSION

Most renal transplant centers use several tests of renal function to monitor the progress of a grafted kidney, but none of these is able to provide a continuous measure of

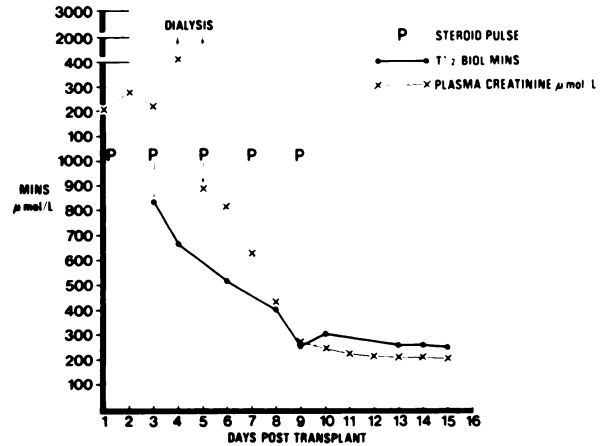


FIG. 7. Comparison between renal clearance of Tc-99m DTPA ($t_{1/2}$) and plasma creatinine levels in patient with normally functioning transplant.

renal function. Computer-processed, scintigraphic time-activity curves give a qualitative and quantitative assessment of renal morphology and function over the time taken to collect the data (usually about 1000 sec), but as this type of renography is only performed relatively infrequently (e.g., once daily), a sudden change in renal function may easily be missed.

Plasma creatinine levels are usually measured daily, so the same criticism applies to them; moreover, as described here, they take at least 24 hr to respond to a change in renal function. On the other hand, continuous or extended external counting using Tc-99m DTPA provides a continuous monitor of renal clearance and indicates any sudden change, such as rupture of the ureteric anastomosis (Fig. 2). From the cases studied, it is also obvious that even the more gradual rejection episodes take place over a period of hours, and valuable time can be saved in instituting treatment (heparin, steroid pulse therapy, etc.).

An additional advantage in using Tc-99m DTPA is that the initial 1000 sec following injection can be used

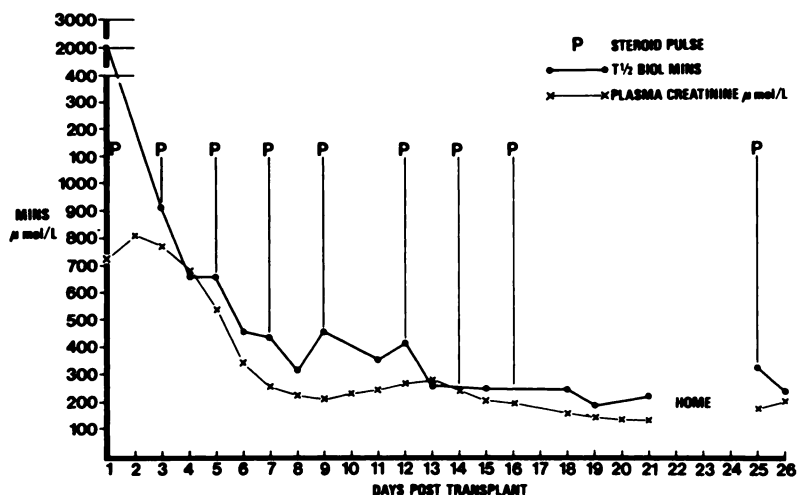


FIG. 6. Comparison between renal clearance of Tc-99m(Sn)DTPA ($t_{1/2}$) and plasma creatinine levels in patient with several rejection episodes that responded to treatment.

to provide daily computer-assisted emission renograms that enable a qualitative assessment of renal morphology and various quantitative measurements of function (e.g., deconvolution) to be performed before external counting begins.

The use of an external counting system involves little expense—for example a single probe from a standard triple-probe renography system can be disconnected and used to perform the serial arm counts at the bedside. No extra staff or training is required since the technicians employed on routine tasks in the transplant ward are fully capable of performing the relatively simple task of recording serial counts and backgrounds. Obviously the routine can be used to most advantage in the immediate posttransplant period and can be continued until the patient leaves the hospital or until irreversible rejection is confirmed.

We conclude that the method described here provides a relatively simple and safe means of monitoring renal function using minimal equipment with little inconvenience to the patient.

FOOTNOTES

* Diagnostic Isotopes Incorp., NJ.

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