COMPARISONS OF ^{99m}Tc-POLYPHOSPHATE AND ^{18}F KINETICS

In the October issue of the *Journal of Nuclear Medicine*, Krishnamurthy, et al (*1*) compared the blood disappearance curves after intravenous injection of ^{18}F and an unspecified ^{99m}Tc-polyphosphate. On the basis of five blood samples per study taken at approximately hourly intervals, they resolved the blood activity curves into two exponential components. This sampling frequency is not sufficient to decide whether the data are best represented by one, two, or more exponentials. Our own data, to be published shortly, employing much more frequent sampling, indicate that the ^{18}F blood disappearance curve is best fitted by a three-component exponential up to 6 hr after injection.

Having extracted two exponentials from their data, Krishnamurthy, et al interpret them as representing bone and renal clearance. This analysis appears to be purely speculative and is almost certainly wrong; since ^{18}F is known to equilibrate rapidly with extraosseous ECF, it is much more likely that the fast exponential predominantly reflects this equilibration. Furthermore, no evidence has yet been presented indicating that the integrated bone uptake of ^{18}F reflects the true clearance. On the contrary, Costeas, et al (*2*) have provided evidence (confirmed in our laboratory) to suggest that there is a marked reflux of ^{18}F from bone.

Twenty years ago it was common practice to attribute individual components of multiexponential curves to single physiologic compartments or processes, but we would suggest that sufficient progress has been made in the mathematical analysis of tracer data to make such an approach appear somewhat naive in the absence of additional experimental data to support the assumptions made.

R. WOOTTON
J. REEVE
Clinical Research Centre
Harrow, Middlesex HA1, 3UJ
England

We want to comment on the article by Krishnamurthy, et al (*1*).

Before studying kinetic data of a labeled compound a definition of the chemical state(s) of the administered radioisotope should be made. Polyphosphate like diphosphate (pyrophosphate) shows differences in organic uptake besides being hydrolyzed by phosphate enzymes in blood and bone (*3,4*). Furthermore, labeling efficiency of different polyphosphate kits with $^{99m}TcO_4^-$ in our experience has a variation of 75–95% from kit to kit. A varying part, therefore, of pertechnetate and reduced but not phosphate-bound technetium will be administered with the ^{99m}Tc-Sn-polyphosphate and in vivo the polyphosphates like the diphosphates will be hydrolyzed (*5*). We use, therefore, a diphosphonate for comparison of the kinetics of a technetium–tin–phosphate complex (*3*). The behavior of the fluoride ion is thought to be fairly consistent (*4*). Unfortunately, the chemistry of "carrier-free" ^{18}F is not well known; there might be less or more complexes with heavy metals (*6*). We use ^{18}F for kinetic studies together with a trace amount of 0.5 mg $Na^{19}F$ to reduce such complexes and to administer a constant amount of fluoride. We also use only preparations of ^{99m}Tc-EHDP which contain less than 2% of nonphosphonate-bound technetium.

The biexponential clearance from plasma in the first 4 hr was seen with these preparations too. Using a weighted least-squares computer fitting, we were able to calculate half-time clearances of both exponents. As we do not believe the first exponent represents bone uptake and the second renal clearance but that the first exponent represents mixture in the distribution volume and exchange with the "slowly exchangeable soft tissue pool" and the second represents both renal and bone clearance, we have studied the half-time clearances in various renal and bone diseases (Table 1).

Neither ^{18}F nor ^{99m}Tc-EHDP are accumulated outside bone or kidney region if there is no tumor, trauma, or infectious disease (*7*). Plasma clearance

TABLE 1. PLASMA CLEARANCE HALF-TIMES FOR EXPONENTS I AND II

Normal and abnormal kidney function	Na-^{18}F		^{99m}Tc-EHDP	
	$T_{I\ 1/2}$	$T_{II\ 1/2}$	$T_{I\ 1/2}$	$T_{II\ 1/2}$
Normal (n = 22)	8.7 ± 1.1	105 ± 14	9.7 ± 1.6	130 ± 21
Reduced kidney function (n = 5)	9.1 ± 2.3	128 ± 14	8.8 ± 2.2	158 ± 13
Without kidney function (n = 4)	8.9 ± 1.8	230 ± 22	8.0 ± 1.8	320 ± 45
Without kidney function with secondary hyperparathyroidism (n = 4)	9.2 ± 2.2	86 ± 25	9.3 ± 1.9	98 ± 35

$\bar{x} \pm s$