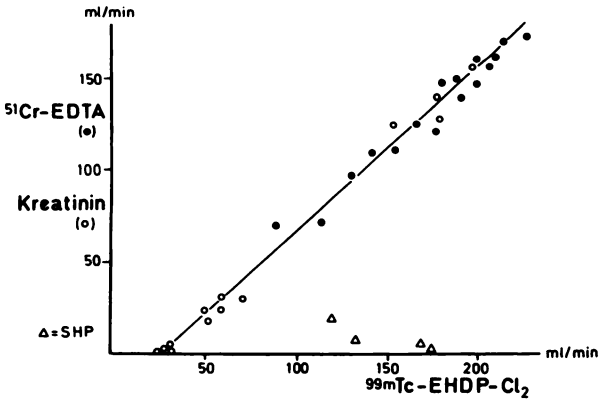

FIG. 1. Comparison of glomerular filtration rate and plasma clearance of ^{99m}Tc-EHDP. y = 0.98x − 30, r = 0.98.

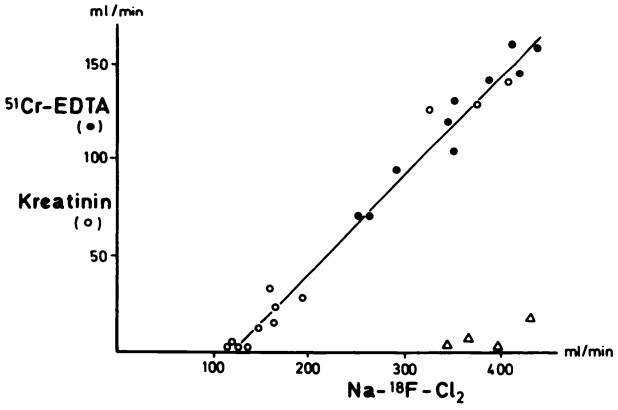

FIG. 2. Comparison of glomerular filtration rate and plasma clearance of ^{18}F. y = 0.47x − 110, r = 0.97.

represents both renal and extrarenal (for practical purposes equal to bone) clearance. This plasma clearance was calculated by the slope/intercept method. There is a significant correlation between glomerular filtration rate and both ^{18}F and ^{99m}Tc clearance (Figs. 1 and 2). In patients without any bone disease, the extrarenal clearance of ^{99m}Tc-EHDP is about 30 ml/min and up to 170 ml/min in patients with renal osteopathy. The corresponding values for ^{18}F are 110 ml/min and 430 ml/min, respectively.

In summary, kinetic studies with labeled compounds should not be done without prior examination of the chemical form(s) of the administered radioisotope. Our results indicate that the first exponent of the biexponential plasma clearance of bone-seeking radioisotopes represents not bone uptake or renal clearance but mixing in the distribution volume. This will be different for different radioisotopes; it is 54 liters/1.73 m^2 body surface using ^{18}F and twice as much as the ^{99m}Tc-EHDP volume ($y = 0.44x$, $p < 0.01$) (*3*).

HANS CREUTZIG
Institut für
Nuklearmedizin
Medizinische Hochschule
Hannover, West Germany

THE AUTHORS' REPLY

We appreciate the interest shown in our study by Wootton and Reeve, and Creutzig. It is an established fact that polyphosphate kits contain many molecules of different chain lengths and that the proportion of any one chain length may vary from batch to batch. We have used polyphosphate kits from two different sources (New England Nuclear and Diagnostic Isotopes) in three separate studies (*1,8,9*). We have carefully avoided introducing oxidizing agents in $^{99m}TcO_4$ solutions before and after adding $^{99m}TcO_4$ to the polyphosphate mixing vials. In three separate studies using different batches of polyphosphate, almost identical kinetic data were obtained indicating that there was no significant variation in the proportions of polyphosphate chain lengths from batch to batch. The salivary glands and stomach were not visualized and only rarely was the thyroid faintly visualized, suggesting that there was no significant in vivo breakdown of the radiopharmaceutical. Only in three instances was there any suggestion of either in vivo breakdown or poor in vitro labeling with diphosphonate (*8*).

In order to avoid the effect of equilibration or mixing on the shape of the blood disappearance curves, we obtained the first blood sample after 10 min. We do not feel that Exponent I is influenced by mixing of the radiopharmaceutical with the blood. In our recent study, we have excluded patients with bone lesions (*10*). In this study, it was found that the blood disappearance curve was, in fact, a composite of three exponentials as suggested by Wootton and Reeve. The clearance half-time of the first rapid component was calculated to be less than 5 min. It should be noted that this component had disappeared before the first 10-min blood sample was drawn in our original studies. Analyses based on the blood disappearance curve indicate that the first two exponents are representative of bone uptake primarily and, to a lesser degree, extraosseous tissue distribution. The third component is thought to represent renal excretion. This analysis is based on the assumption that, after uptake, there is no clearance of the radiopharmaceutical from the bone. This assump-

tion has been confirmed in a recent study by Weber, et al (*11*).

G. T. KRISHNAMURTHY
M. TUBIS
W. H. BLAHD
VA Wadsworth Hospital Center, and
UCLA School of Medicine
Los Angeles, California

REFERENCES

1. KRISHNAMURTHY GT, THOMAS PB, TUBIS M, et al: Comparison of ^{99m}Tc-polyphosphate and ^{18}F. I. Kinetics. *J Nucl Med* 15: 832–836, 1974

2. COSTEAS A, WOODARD HQ, LAUGHLIN JS: Depletion of ^{18}F from blood flowing through bone. *J Nucl Med* 11: 43–45, 1970

3. CREUTZIG H: Vergleichende Untersuchungen mit osteotropen Radionukliden. II. Clearance von Fluor-18 und Technetium-99m-EHDP: in press

4. WELLMAN HN, BROWNE A, KAVULA M, et al: Optimization of a new kit-prepared skeletal imaging agent, ^{99m}Tc-Sn-EHDP, compared with ^{18}F. In *Radiopharmaceuticals and labelled compounds*, vol 1, Vienna, IAEA, 1973

5. JUNG A, RUSSELL RGG, BISAZ S, et al: Fate of intravenously injected pyrophosphate-32P in dogs. *Am J Physiol* 218: 1757–1764, 1970

6. BERSIN TH: Biochemie der Mineral- und Spurenelemente, Stuttgart, Akademische Verlagsgesellschaft, 1963

7. CREUTZIG H: Bone scanning in malignant and nonmalignant disease. Fluor versus Technetium: in press

8. KRISHNAMURTHY GT, TUBIS M, ENDOW JS, et al: Clinical comparison of the kinetics of ^{99m}Tc-labeled polyphosphate and diphosphonate. *J Nucl Med* 15: 848–855, 1974

9. KRISHNAMURTHY GT, HUEBOTTER RJ, WALSH CF, et al: The kinetics of ^{99m}Tc-labeled pyrophosphate and polyphosphate in man. *J Nucl Med* 16: 109–115, 1975

10. GRAHAM LS, KRISHNAMURTHY GT, BLAHD WH: Compartment models and the radiation absorbed dose for three technetium-labeled skeletal-seeking radiopharmaceuticals: Manuscript in preparation.

11. WEBER DA, KEYES JW, BENEDETTO WJ, et al: ^{99m}Tc pyrophosphate for diagnostic bone imaging. *Radiology* 113: 131–137, 1974

EFFECTS OF TIN ON PERTECHNETATE DISTRIBUTION

A specifically abnormal imaging pattern has been observed consistently when ^{99m}Tc-pertechnetate brain imaging followed ^{99m}Tc-stannous pyrophosphate imaging using the Mallinckrodt TechneScan PYP kit. The abnormal brain pattern shows disproportionately increased activity in the vascular structures such as the superior sagittal sinus, transverse sinus, and the region of the choroid plexi, in spite of potassium perchlorate "blocking" prior to isotope injection. The abnormal torso pattern shows increased activity in the kidneys, liver, and the vascular structures of heart, aorta, and peripheral vessels such as the iliacs, femorals, and subclavians. We are not visualizing the usual pertechnetate activity that should be present in the gastric mucosa and salivary glands.

One recent brain scan preceding a bone scan showed a large "hot" right parietal metastasis from a bronchogenic carcinoma. When the pertechnetate brain scan was repeated following an interim bone scan, the positive cerebral metastasis became nondetectable.

During pertechnetate imaging that follows bone imaging, in vitro testing shows a 30-fold increase of technetium activity in the erythrocytes compared to plasma. These findings strongly suggest in vivo intracellular reduction of technetium pertechnetate with permanent labeling to large intracellular molecules. These data in humans correlate with McRae, et al (*1*) and Steigman, et al (*2*) and suggest the stannous content in the Mallinckrodt TechneScan PYP kit may be unacceptably high. Closer scrutiny of the stannous ion content in bone-imaging kits as well as further research on the toxicity or metabolic effects of Sn(II) appear to be necessary.

WILLIAM M. CHANDLER
LORRI D. SHUCK
Fairview Hospitals
Minneapolis, Minnesota

THE AUTHOR'S REPLY

Chandler and Shuck point out an abnormal imaging pattern when ^{99m}Tc-pertechnetate brain imaging follows bone imaging using the Mallinckrodt TechneScan PYP kit. This kit is labeled as containing 15.4 mg stannous pyrophosphate and calculation implies a Sn(II) content of 8.94 mg. Assuming that a 70-kg man receives one-fifth the contents of the vial of prepared pyrophosphate, the dose of tin approximates 0.02 mg Sn(II)/kg which is included in the dose response curve shown in Fig. 3 of a paper by McRae, et al (*1*). Very definite changes in pertechnetate metabolism are to be expected in patients previously studied with this agent.

JAMES McRAE
University of California, Berkeley
Berkeley, California

REFERENCES

1. MCRAE J, SUGAR RM, SHIPLEY B, et al: Alterations in tissue distribution of ^{99m}Tc-pertechnetate in rats given stannous tin. *J Nucl Med* 15: 151–155, 1974

2. STEIGMAN J, RICHARDS P: Chemistry of technetium 99m. *Semin Nucl Med* 4: 269–279, 1974