# $^{99m}$Tc-Pyrophosphate in Demonstrating Bone Disease of Parathyroid Dysfunction

The incidence of bone disease in dysfunctional parathyroid states varies with the duration of the primary disease and the apparent excess or deficiency of parathyroid hormone (PTH). In primary hyperparathyroidism the histologic assessment of random bone samples reveals widespread disease in more than 90% of the cases. However, only 30% of these patients show nonspecific generalized qualitative osteopenia on conventional skeletal x-rays. More specific focal x-ray changes (i.e., cortical subperiosteal resorption, absence of lamina propria, Brown tumors, cysts) are even more uncommon and appear in approximately 10% of hyperparathyroid patients.

The obvious insensitivity of the x-ray in revealing the presence and extent of bone involvement in hyperparathyroidism has led a small number of investigators to evaluate the efficacy of bone-seeking radiopharmaceuticals in this condition (*1,2*). Two articles in this issue of the *Journal* address this problem by quantifying the biologic fate of $^{99m}$Tc-stannous pyrophosphate ($^{99m}$Tc-PP$_i$) in primary and secondary hyperparathyroid patients. Using the activity ratio of distal femur bone to soft tissue at 5 hr after the administration of $^{99m}$Tc-PP$_i$, Weigmann et al. (pp 231–235) found no difference between their normal and primary hyperparathyroid patients. Eighty percent of their bone images were normal or near normal, and yet more than 50% of these patients showed focal extremity subperiosteal resorption and/or extensive osteopenia. None of the patients showed elevated serum alkaline phosphatase levels. All of the uremic patients with secondary hyperparathyroidism showed elevated bone-to-soft-tissue ratios, abnormal bone images, and focal x-ray subperiosteal resorption. As a result of their study, Wiegmann et al. concluded that $^{99m}$Tc-PP$_i$ is even less of an indicator of bone disease than the skeletal x-ray. They explain the increased bone-image uptake to the nonspecific binding of the radiopharmaceutical to abnormal (immature) collagen, which occurs in conditions other than primary hyperparathyroidism [i.e., vitamin D deficiency, chronic renal disease (*3*)].

In addition to bone imaging with $^{99m}$Tc-PP$_i$ in patients with primary hyperparathyroidism, Krishnamurthy et al. (pp 236–242), measured its clearance from the blood and its urinary excretion rate. Several postsurgical untreated hypoparathyroid and pseudohypoparathyroid patients were also studied. The radiometabolic studies were compared to the skeletal x-ray and correlated with $^{125}$I absorptimetric bone-mineral measurements. The blood disappearance curves of $^{99m}$Tc-PP$_i$ were identical in all three groups. Significant increased urinary excretion of $^{99m}$Tc-PP$_i$ activity was recorded, mainly during the first hour, in the hyperparathyroid and pseudohypoparathyroid groups. The $^{99m}$Tc-PP$_i$ bone images were abnormal in 58% of the hyperparathyroid patients, and the lesions were confined to the distal extremities, skull, and mandible. Half of these patients showed x-ray changes of subperiosteal resorption and osteopenia, but only a quarter showed $^{99m}$Tc-PP$_i$ image correlation. Only one of the x-rays and two of the images showed good correlation with the bone mineral measurements in the hyperparathyroid patients. The authors attributed their findings of early increased $^{99m}$Tc-PP$_i$ urinary excretion to the excess circulating PTH and its effect on the kidney and implied that the focal increased skeletal uptake of $^{99m}$Tc-PP$_i$ is also mediated by PTH activation of osteoprogenitor cells and the presence of immature collagen in this disease. One might deduce from their overall results a greater,

although only slight, sensitivity for $^{99m}$Tc-PP$_i$ than for the bone x-ray studies. However, this preference is not overtly espoused by the authors.

Neither report completely excludes or establishes $^{99m}$Tc-PP$_i$ studies as a true indicator of hyperparathyroid bone disease. The major reason is the obvious lack of knowledge or clear understanding of the precise mechanism of how the $^{99m}$Tc-labeled phosphates are accumulated (accretion) by bone. Bone blood flow contributes by delivering the radiopharmaceutical and, depending on the local environment, exposes it to a large surface area. The radiopharmaceutical clears from the blood biexponentially with a rapid early phase that probably distributes throughout the entire extracellular space and a slower later phase that goes intracellularly and preferentially to bone (Charkes ND: personal communication). The bone accretion rate of the agents by bone appears to be constant and is mediated by several factors (i.e., humoral, enzymes), one of the more important being PTH. As Krishnamurthy has shown, even in the face of excess circulating PTH the $^{99m}$Tc-PP$_i$ accretion rate appears to be constant and the renal effect of PTH is manifested by the greater urinary excretion of $^{99m}$Tc-PP$_i$.

Although the propensity of $^{99m}$Tc-PP$_i$ for immature collagen is suggested by both authors, the results are only subjective. Zimmer et al. (*4*) have shown enzymatic receptor binding of the radiopharmaceutical in vitro, and at present this is as plausible a consideration.

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*3.* ROSENTHALL L, KAYE M: Observations on the mechanism of $^{99m}$Tc-labeled phosphate complex uptake in metabolic bone disease. *Semin Nucl Med* 6: 59–67, 1976

*4.* ZIMMER AM, ISITMAN AT, HOLMES RA: Enzymatic inhibition of diphosphonate: A proposed mechanism of tissue uptake. *J Nucl Med* 16: 352–356, 1975

## BOOKS RECEIVED

The receipt of the following books is acknowledged:

*Atlas of Cerebrovascular Disease.* William F. McCormick and Sydney S. Schochet, Jr. 422 pp, illustrated. Philadelphia, W. B. Saunders Co., 1976. $28.00.

*Graphs and Tables for Use in Radiology.* F. Wachsmann and G. Drexler, 240 pp. New York, Springer-Verlag, 1976. $19.70.

*Cerebral Radionuclide Angiography.* Frank H. DeLand, 309 pp, illustrated. Philadelphia, W. B. Saunders Co., 1976. $39.75.

*The Basic Physics of Radiation Therapy, 2nd ed.* Joseph Selman. 742 pp. Springfield, Ill., C.C. Thomas, 1976. $25.75.

*The Physical Aspects of Radioisotopic Organ Imaging.* K. G. Leach. 25 pp, illustrated. London, British Institute of Radiology, 1976. £1.50.

*Introduction to the Principles of Diagnostic Ultrasound.* H. B. Meire and P. Armstrond. 13 pp, illustrated. London, British Institute of Radiology, 1976 £1.40

*Fundamental Aspects of Medical Thermography.* W. M. Park and B. L. Reece. 36 pp, illustrated. London, British Institute of Radiology, 1976. £3.40.