Reply

Dr. Schneider's major objection is the use of fixed doses of radioactive iodine. He has enumerated several factors that must be taken into consideration if one is to calculate a specific thyroidal dose. In our article we enumerated some other factors, not dependent on uptake or thyroid size, that influence the incidence of hypothyroidism. There is in addition an individual variation in patient response not accountable for by any known factor. For these reasons we abandoned several years ago the type dose calculation he advocates.

Neither our hypothyroid contrasted with euthyroid, nor our blocker-treated contrasted with untreated, groups differed significantly in either radioactive iodine uptake or gland size. Specifically, the patients with the 16% and 83% uptakes were both men in their mid-30's with glands 2½ times the normal size. Neither had been treated with blockers and neither developed hypothyroidism. The next highest uptake was 81% in a man, pretreated with thyroid blockers, whose gland was three times normal size. He did not become hypothyroid.

As far as we could determine, the patients in studies that we compared with ours were similar to ours in gland sizes and uptakes. It must be remembered that we are comparing *groups* of patients treated in the same fashion. We therefore do not believe that failure to calculate specific thyroidal doses negates any of our conclusions.

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Use of Whole-Body Retention of Tc-99m Diphosphonate in the Diagnosis of Metabolic Bone Disease

The paper by Dr. Fogelman et al. (*1*) in this journal's March issue presents much-needed data regarding differing backgrounds, bone uptake, blood levels, and whole-body retentions in various metabolic diseases of bone. We have recent kinetic results indicating that bone retention of Tc-99m-HEDP after the first few hours (following the washout of exchangeable or reversibly bound activity) is proportional to the integral of the blood or plasma activity (*2*). It occurs to us that Dr. Fogelman's excellent data could be more meaningfully expressed in terms of liters of plasma cleared of the agent by the skeleton per hour—a quantitative expression of the total ability of the skeleton to concentrate the bone agent, independent of renal excretion. We have graphically integrated Dr. Fogelman's blood curves over 24 hours and divided them into his average 24-hr retention values to yield the suggested clearance values (see Table 1). This procedure not only normalizes the data for the influence of differing renal excretion rates, but also gives a direct measure of a metabolic parameter of the skeleton. We are still not completely clear as to the mechanism of irreversible fixation of the agent in bone, but presume it is related to the deposition of new bone, as well as to other factors. It is assumed in our calculations that at 24 hours the soft-tissue retention contributes only negligibly to the whole-body retention.

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2. ARNOLD JS, BARNES WE, KHEDKAR N, et al: Computerized kinetic analysis of two 99m-Tc-Sn-diphosphonates demonstrating different binding characteristics. *J Nucl Med* 19: 740, 1978 (abst)

Reply

Further to Dr. Arnold's interesting treatment of our data on 24-hr whole-body retention (WBR) and plasma concentration of Tc-99m HEDP, we have carried out similar calculations of skeletal clearance for each of 48 patients with metabolic disease and 13 control subjects. (We have availed ourselves of some results obtained since our paper was submitted.) We derived the area under the plasma activity-time curve for each subject by fitting a double exponential to the data points by an iterative least-squares procedure. The skeletal plasma clearance of Tc-99m HEDP was obtained directly from the fitted parameters of the plasma curve and the 24-hr WBR. Our results are seen in Table 1. Using the Wilcoxon rank-sum test, the control group was found to be significantly different from the Paget's, renal osteodystrophy, and osteomalacia groups ($p < 0.001$). There was no significant difference between the con-

TABLE 1

Disease	% dose retained at 24 hr	Integral of plasma curve 0–24 hr % dose-hr/liter	Plasma clearance ml/hr
Normal	19.2	29.8	644
Osteoporosis	21.2	40.6	500
Hyperparathyroidism	50.7	54.0	939
Osteomalacia	40.7	33.3	1222
Renal osteodystrophy	88.6	48.4	1831
Paget's disease	56.9	25.2	2258

TABLE 1. SKELETAL PLASMA CLEARANCE OF Tc-99m HEDP

Group	Number	Plasma clearance ml/hr Mean ± s.d.	Absolute range
Normal	13	684 ± 169	296– 948
Osteoporosis	9	687 ± 229	459–1150
Primary hyperparathyroidism	8	946 ± 302	534–1429
Osteomalacia	8	1836 ± 844	995–3593
Renal osteodystrophy	11	2229 ± 1207	1099–5475
Paget's disease	12	2233 ± 897	885–3904

trol group and the osteoporotic group, and the difference from the primary hyperparathyroidism group was only significant at the 5% level. There was no overlap between individual patients in the control group and those in the renal osteodystrophy and osteomalacia groups. Only one patient in the Paget's group, but four (50%) in the primary hyperparathyroidism group, fell within the absolute control range.

Although skeletal plasma clearance is an interesting measure, which would be expected to reduce the influence of varying real function, we are uncertain as to its exact meaning or clinical application. Individual patients with primary hyperparathyroidism can be clearly differentiated from control subjects by the 24-hr WBR of Tc-99m HEDP, and in our opinion this test provides a more sensitive indicator of skeletal disease.

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The Predictive Value of Myocardial Perfusion Scintigraphy after Stress in Patients without Previous Myocardial Infarction

The article by Turner et al. (*1*) is certainly an excellently conceived study, but it is unfortunate that there is a grave limitation in the method of imaging these patients. The use of Polaroid film with the inherent lack of contrast that hard-copy radiographs offer, and the lack of computer manipulation—specifically, nine-point smoothing and background subtraction—severely limit the ability to interpret myocardial perfusion studies. If one is exposed to both modalities, one would hardly choose the Polaroid photographs as a basis for interpretations. It is unfortunate that this is the only modality available in the study, and I am convinced it has diminished the value of the work. I hope that future studies in this exciting new aspect of nuclear medicine are not limited by imaging methods using Polaroid studies without some form of processing as described.

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REFERENCE

1. TURNER DA, BATTLE WE, DESHMUKH H, et al: The predictive value of myocardial perfusion scintigraphy after stress in patients without previous myocardial infarction. *J Nucl Med* 19: 249–255, 1978

Reply

We are pleased that Dr. Cusmano regards our study as "excellently conceived," although he obviously has doubts about the excellence of its execution.

Thallium-201 images on transparent display media are subjectively more appealing than Polaroid images. One should not, however, assume that this necessarily translates into superior detectability of disease. We usually acquire Tl-201 images simultaneously on transparent (Kodak RP) and Polaroid films; and although we have not compared observer performance with these two media in a rigorous manner, it is our impression that perfusion defects "seen" in images recorded with one medium can always be readily appreciated in images recorded with the other. At first glance, this may seem surprising. On theoretical as well as empirical grounds, however, one would not expect contrast enhancement to offer much advantage in the interpretation of images of low count density (*1*). Furthermore, distinguishing normal from abnormal variations in the distribution of Tl-201 in images of the myocardium may be more of a problem than detection of those variations.

Dr. Cusmano's conviction that processing of Tl-201 images makes a world of difference in observer performance is shared by others. His criticism, however, should be tempered by the knowledge that objective evidence to support this thesis is hard to come by: as of this writing, no well-designed observer performance experiment comparing processed and unprocessed Tl-201 imaging has been published. Nonetheless, we recognize the possibiilty that image processing may have improved the inherent detectability of myocardial perfusion abnormalities in our series, and, in fact, we dealt with this possibility in our paper (*2*). As we have noted therein, it would have taken a very great increase in sensitivity to alter our conclusions: the sensitivity of Tl-201 scintigraphy would have to be close to 95% (with a specificity of 97%) in order to apply the test confidently as a pre-angiographic screening procedure for patients with a prior probability of coronary artery disease as high as 50%, e.g., patients with atypical angina pectoris (*3,4*). Furthermore, even if processing of Tl-201 perfusion scintigrams were to result in a sensitivity as high as 95% with a specificity of 97%, its application as a pre-angiographic screening test would be inappropriate for patients with typical angina pectoris: the predictive value of a negative test would be only about 50%, because the prevalence of significant coronary artery disease in this population is approximately 95% (*3,4*).

The foregoing reasoning leads us to the conclusion that even if processing of Tl-201 images proves to be as marvelous as Dr. Cusmano thinks it is, he and the rest of us had better apply Tl-201 scintigraphy selectively, or we will be making large numbers of false-negative diagnoses. That is the essence of the "message" of our paper, and we do not believe that the use of transparent display media or any amount of image processing will, as Dr. Cusmano suggests, "diminish the value" of that message.

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4. MCCONAHAY DR, MCCALLISTER BD, SMITH RE: Post-exercise electrocardiography: Correlation with coronary arteriography and left ventricular hemodynamics. *Am J Cardiol* 28: 1–9, 1971

Platelet Contamination of Radioactive Colloid Labeled Leukocyte Preparations

Human leukocytes labeled with gamma-emitting isotopes are potentially useful for detecting sites of inflammation