REPLY: We agree that our use of the word "dose" might be confusing. We were using it in the common clinical sense, as in Solomon's statement that "Despite the many complicated schemes for determining the dose of radioactive iodine to administer . . . variability in uptake and ultimate response foils the most elegant methods to standardize the delivery of radiation to the thyroid gland" (*1*). From a pure radiobiologic point of view, the word "dose" might be reserved for the energy deposited in the thyroid gland; for practical purposes, "administered activity" or "administered dose" might be used for the amount given orally.

We hope, however, that this use of words will not obscure our fundamental aim, which was not "to make the patient hypothyroid without total ablation," but to provide choices for both physicians and patients when the desired endpoint is cure of hyperthyroidism.

Solomon (*1*) defines two major schools of thought regarding the treatment of hyperthyroidism with ^{131}I that imply different values and goals. In the first approach, "one administers a dose of ^{131}I calculated to produce hypothyroidism in most recipients," with rapid cure of hyperthyroidism as the central goal. It assumes that hypothyroidism will occur in the long run for most patients regardless of administered dose, and therefore its development is of less concern. When about 15 mCi is administered, the percent cure is about 95% (*2*). In the second approach, "one administers a dose calculated to have the best chance of resulting in a cure, with the lowest combined incidence of hypothyroidism and persisting hyperthyroidism." Using a dose calculated to meet this set of goals, the mean percent cure has remained at about 70% for the past 40 years (1950–1990) (*3*).

Each of these methods has its proponents, and each may be used for individual patients under different circumstances. Our efforts were to de-emphasize the dichotomy by providing a better understanding of the direct relationship between administered dose and both cure of hyperthyroidism and early (but not delayed) development of hypothyroidism. This information provides patients and physicians alike with a clearer choice between administered dose and the likelihood of persisting hyperthyroidism with its increased disability and cost.

REFERENCES

1. Solomon DH. Treatment of Graves' hyperthyroidism. In: Ingbar SH, Braverman LE, eds. *Werner's the thyroid, fifth edition.* Philadelphia: Lippincott; 1986:1001–1005.
2. Nordyke RA, Gilbert FI Jr. Optimal iodine-131 dose for eliminating hyperthryoidism in Graves' disease. *J Nucl Med* 1991;32:411–416.
3. Nordyke RA, Gilbert FI Jr. Unpublished literature compilation of 10,213 hyperthyroid patients from 48 studies.

Robert A. Nordyke
Fred I. Gilbert, Jr.
Straub Clinic & Hospital
Honolulu, Hawaii

Assessment of Myocardial Infarction with Three Radiotracers

TO THE EDITOR: Henrich et al. (*1*) compared myocardial accumulation of ^{201}Tl, fluorodeoxyglucose (FDG) and a type of ^{123}I-pentadecanoic acid (oPPA) in 32 patients with recent myocardial infarction in the July issue of the *Journal*. The authors are correct in that they measured uptakes rather than metabolic rates of FDG.

There are, however, some areas in this paper that need clarification.

1. One of the problems with this work is that the authors did not perform reinjection of ^{201}Tl to uncover viable myocardium. As Bonow et al. have demonstrated, reinjection induces ^{201}Tl uptake in many segments that show fixed defects on conventional ^{201}Tl scintigraphy (*2*). The power of the reinjection method is probably based on reversion of the unavoidable fall in ^{201}Tl concentration in the blood (*3*). Of course, this problem does not exist when imaging with hexamibi or teboroxime, since two separate injections of radiopharmaceutical are required. Why were these data submitted without reinjection results?
2. Equally bothersome is the absence of a gold standard for definition of infarct size, a parameter which ultimately is critical for prognostication in these patients. Incidentally, and for clinical research purposes, wall thickening assessment (preferably using the three-dimensional volume element approach) is superior to conventional wall motion analyses in distinguishing ischemic from nonischemic zones and in mapping regional function (*4*).
3. Interestingly, of the 128 myocardial quadrants in the 32 patients with fixed ^{201}Tl defects, only 13 were akinetic (Table 1). Of these 13, only 7 had normal FDG uptake, i.e., 7/128 of quadrants (=5%) were akinetic and had normal FDG uptake. Of the 408 myocardial segments with fixed ^{201}Tl defects, 160 (=39%) had normal FDG uptake (Table 2). No wall function data are given for segments.
   Subsequently, we have no idea about infarct size, and there are disparate results for quadrants and segments.
4. The scattergram shown in Figure 3 is not particularly revealing. Theoretically, there is an inverse relationship between uptake of glucose and of free-fatty acids (*5*). In this work, the metabolic conditions at the time of the FDG study and at the time of oPPA study were vastly different (i.e., oral glucose versus overnight fast). While the authors see a correlation between FDG and oPPA uptakes in Figure 3, many would disagree with this assertion.
5. The authors conclude by saying that a minor number of segments showed FDG uptake only, indicating a tendency toward glycolysis and inhibition of fatty acid uptake. Many investigators have now confirmed the data of Liedtke et al. (*6*) that in the reperfused heart fatty acids, not glucose, are the preferred substrate for myocardial oxidation leading to generation of ATP. FDG, in any case, is a poor tracer of the glycolytic pathway (*7*).

REFERENCES

1. Henrich MM, Vester E, von der Lohe E, et al. The comparison of 2-^{18}F-2-deoxyglucose and 15-(ortho-^{123}I-phenyl)-pentadecanoic acid uptake in persisting defects on thallium-201 tomography in myocardial infarction. *J Nucl Med* 1991;32:1353–1357.
2. Bonow RO, Dilsizian V, Cuocolo A, et al. Identification of viable myocardium in patients with chronic coronary artery disease and left ventricular dysfunction. *Circulation* 1991;83:26–37.
3. Budinger TF, Knittel BL. Cardiac thallium redistribution and model. *J Nucl Med* 1987;28:588.
4. Azhari H, Sideman S, Weiss JL, et al. Three-dimensional mapping of acute ischemic regions using MRI: wall thickening versus motion analysis. *Am J Physiol* 1990:H1492–H1503.

5. Opie LH, ed. *The Heart*, second edition. New York: Raven Press; 1991:26.
6. Liedtke AJ, DeMaison L, Eggleston AM, et al. Changes in substrate metabolism and effects of excess fatty acids in reperfused myocardium. *Circ Res* 1988;62:535–542.
7. Renstrom B, Nellis SH, Liedtke AJ. Metabolic oxidation of pyruvate and lactate during early myocardial reperfusion. *Circ Res* 1990;66:282–288.

J. A. Bianco
University of Wisconsin
Madison, Wisconsin

REPLY: My response to the concerns raised by Dr. Bianco are as follows.

1. Our study (*1*) compared FDG with fatty acid uptake in infarcted areas. Additional information concerning ^{201}Tl reinjection would certainly be of interest. In this study, we were limited to the injection of three radioactive tracers. Thallium-201 reinjection would have increased considerably the radiation dose received by the patients.
2. We are in agreement with Dr. Bianco that the comparison between wall motion obtained from ventriculography and scintigraphy by PET and SPECT has its limitations. Nevertheless, it is currently a widely accepted and available method.
3. Because of the above-mentioned difficulty of comparing functional and scintigraphic data, a division of the heart into quadrants was chosen for the comparison of wall motion and scintigraphic data, whereas for the comparison of various scintigraphic data, smaller segments (41 segments per heart) were used. The finding of disparate results by Dr. Bianco was the result of misreading. As we state in the second sentence in the Results section: "Of a total of 128 analyzed quadrants 43 (34%) exhibited ^{201}Tl defects in the redistribution tomogram. Out of these, 23 (53%) had low FDG and oPPA uptake, 13 (30%) normal FDG and oPPA uptake, 1 (2%) low FDG but normal oPPA, and 6 (14%) normal FDG but low oPPA uptake." This means that 19/43 (44%) quadrants with a defect in the ^{201}Tl redistribution tomogram exhibited normal FDG uptake. This is in agreement with 39% in the case of myocardial segments.
4. The negative correlation between free-fatty acid concentration in plasma and myocardial glucose uptake (*2,3*) is well known. The aim of the study was to evaluate the merit of scintigraphy using the iodinated fatty acid derivative oPPA against that using FDG under the metabolic condition that is technically best suited for each scintigraphic procedure. This was done by fasting in the fatty acid studies and by elevating the insulin level (by glucose load) in the FDG studies. Obviously, insulin is the major determinant of FDG uptake. The positive correlation between oPPA and FDG uptake in ^{201}Tl redistribution defects under these metabolic conditions is moderate, but significant.
5. The paper of Liedtke et al. (*4*) referred to by Dr. Bianco reports an increase of palmitate oxidation after relatively mild ischemia (60% flow reduction during 45 min) followed by 1 hr of reperfusion. Fatty acid uptake was not determined in this study. It is improbable that this experimental model characterizes the metabolic situation in patients who have had a myocardial infarction more than 4 wk prior to the study. Furthermore, oPPA traces mainly fatty acid uptake and only a minor proportion undergoes β-oxidation (*5*). Schwaiger et al. (*6*) reported that in the fasting state about one-third of the glucose extracted by the myocardium immediately enters the glycolytic pathway under control conditions. After a 3-hr occlusion and 24-hr reperfusion, the extraction of glucose increased, whereas that of nonesterified fatty acids decreased. About two-thirds of the glucose, which is extracted by the myocardium under this condition, immediately enters the glycolytic pathway. Additional studies using ^{11}C-palmitate also showed a depressed fatty acid uptake to various extents during reperfusion (*7,8*).

In general, the suitability of a tracer as a marker of myocardial viability probably depends on more complex factors, not primarily whether the substrate is the preferential one for reperfused areas. In comparison to the regional myocardial uptake of FDG, the uptake of fatty acids is, for example, much more dependent on myocardial blood flow due to the lower extraction fraction of FDG.

REFERENCES

1. Henrich MM, Vester E, von de Lohe E, et al. The comparison of 2-^{18}F-2-deoxyglucose and 15-(ortho-^{123}I-phenyl)-pentadecanoic acid uptake in persisting defects on thallium-201 tomography in myocardial infarction. *J Nucl Med* 1991;32:1352–1357.
2. Randle PJ, Garland PB, Hales CN, Newsholme EA. The glucose fatty-acid cycle. *Lancet* 1963;i:785–789.
3. Wisneski JA, Gertz EW, Neese RA, et al. Metabolic fate of extracted glucose in normal human myocardium. *J Clin Invest* 1985;76:1819–1827.
4. Liedtke AJ, DeMaison L, Eggleston AM, Cohen LM, Nellis SH. Changes in substrate metabolism and effects of excess fatty acids in reperfused myocardium. *Circ Res* 1988;62:535–542.
5. Kaiser KP, Geuting B, Grobmann, et al. Tracer kinetics of 15-(ortho-$^{123/131}$I-phenyl)-pentadecanoic acid (oPPA) and 15-(para-$^{123/131}$I-phenyl)-pentadecanoic acid (pPPA) in animals and man. *J Nucl Med* 1990;31:1608–1616.
6. Schwaiger M, Neese RA, Araujo, L et al. Sustained nonoxidative glucose utilization and depletion of glycogen in reperfused canine myocardium. *J Am Coll Cardiol* 1989;13:745–754.
7. Schwaiger M, Schelbert HR, Ellison D, et al. Sustained regional abnormalities in cardiac metabolism after transient ischemia in the chronic dog model. *J Am Coll Cardiol* 1985;6:336–347.
8. Knabb RM, Bergman SR, Fox KAA, Sobel BE. The temporal pattern of recovery of myocardial perfusion and metabolism delineated by positron emission tomography after coronary thrombolysis. *J Nucl Med* 1987;28:1563–1570.

Michael M. Henrich
Institute of Medicine
Research Center Julich
Julich, Germany

Development of New Radiopharmaceuticals

TO THE EDITOR: This letter is addressed to all my colleagues in the field of nuclear medicine for their consideration and contemplation.

I have been directly involved in the commercial development of new radiopharmaceuticals for 25 years. I have lived through the transition from virtual freedom in the practice of nuclear medicine to the current restrictive environment. I now want to share with you some of my experiences, insights and perspectives.

The current regulations and restrictions imposed on the practice of nuclear medicine significantly impede growth. However, regulatory agencies are not the greatest impediment to the growth