cost from retreatment with radioiodide as well as from "... extended disability and income loss..." To this we have to add expenses from possible anti-thyroid drugs in the interim as well as potential side effects from these medications.

3. The results of retreatment with radioiodide have been analyzed in some detail (3). If we define "cured" of hyperthyroidism as being euthyroid or hypothyroid, then expressions are available for describing the results as a function of the quantity of radioiodide administered. Each physician must determine for herself/himself what fraction of patients they wish to cure with a single dose of radioiodide, while leaving the remainder still hyperthyroid. Choices between radiation exposure, prolonged disease, and possible side effects of anti-thyroid drugs are not easy to make. If evidence mounts of the relative "benign" nature of larger doses of oral radioiodide, therapy of hyperthyroidism will be simplified.

REFERENCES

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REPLY: Dr. Spencer's thoughtful comments and general agreement with our approach to the treatment of hyperthyroidism with radioiodide are appreciated. Although not stated in our article (1), we agree that the use of anti-thyroid drugs both before and after treatment with 131I adds to the cost and risk for many patients. Dr. Spencer states that the choice between radiation exposure and prolonged hyperthyroidism will be simplified "if evidence mounts of the benign nature of larger doses of oral radioiodide." Perhaps so. In the meantime, we feel that our approach is simple enough. It clearly lays out the probability of cure of hyperthyroidism versus the amount of radioiodide administered. This allows both the physician and the patient to participate in the decision of how much radioiodide to use. Such informed decisions should be a major concern of both physicians and patients (2).

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REFERENCES

The Difference in Clearance Between Kit-Prepared Technetium-99m-MAG3 and Radioiodinated Hippuric Acid

TO THE EDITOR: Müller-Suur et al. (1) reported that the renal clearance of kit-prepared 99mTc-MAG3 was lower than that of 123I-labeled o-iodohippuric acid (OIH) by about 50%. These results were based on studies in only 17 patients, who were examined at intervals of 2–8 days, as opposed to our simultaneous investigations in 124 patients using HPLC-purified 99mTc-MAG3, under steady-state conditions (2,3). Their clearance calculations were performed during slope with the aid of totally different methods, and additionally, the radiochemical purity of 95% was not verified by HPLC but by a simplified method (4).

The renal clearances of different radiopharmaceuticals can be compared with each other only if the measurements are per-
formed simultaneously and not sequentially, due to the fact that physiologic variations and circadian rhythms of the renal function substantially influence the results (5,6). Since clearances should be determined during steady-state or at least be calculated according to the same model, the regression coefficients indicated by Müller-Suur et al. (1) concerning the relation of the 99mTc-MAG3 clearance to the OH clearance cannot be considered to be representative. Another requirement in this context should have been the precise determination of the radiochemical purity of the agent by HPLC.

Müller-Suur et al. presumed that the clearance of 99mTc-MAG3 was lower than that of OIH, due to a lower gomerularly filtered portion and a lower renal secretory transport capacity of 99mTc-MAG3. The filtration fraction of the human kidney, which amounts to 20%, only considers the “free” (i.e. the non-protein-bound) fraction in the plasma. Therefore, only 6% of OIH (protein binding ~ 70%) and 2% of 99mTc-MAG3 (protein binding 90%) are eliminated by glomerular filtration (2,3,7), which implies that the differences are insignificant. As opposed to the statement by Müller-Suur et al. (1) asserting that other authors have observed a lower secretory transport capacity of 99mTc-MAG3 as compared to OIH, these reports, and particularly the paper published by our group (8) and quoted by Müller-Suur, deal with studies regarding the affinity of the respective radio-pharmaceuticals to the tubular transport system. The maximum transport capacity of the tubular cell (Tm) represents a totally different parameter which, until now, has not been determined for 99mTc-MAG3 due to the fact that no technetium isotope is available for in vivo application in amounts of several grams. We assume that the higher plasma protein binding of 99mTc-MAG3 is the main reason for the lower clearance of this agent, as compared with OIH, because the peritubular transit time is too short for complete dissociation of 99mTc-MAG3 from the plasma protein so as to be available for the active tubular transport (2,3).

Furthermore, Müller-Suur et al. state that it has been reported that the “whole-blood clearance for MAG3 was found to be the same or even higher (7,9) than that for hippurate.” This is incorrect: Coveney and Robbins (9) performed their studies in rats, which have a different binding to plasma proteins and to red blood cells (RBCs) than humans, and Taylor et al. (7) obtained results in their sequential study, which were based on an error, later discovered by the authors, concerning decay corrections (10). According to our results (2,3), the relation between the whole-blood clearances of 99mTc-MAG3 and OIH is higher than the relation between the respective plasma clearances by a factor which can be calculated precisely, taking into account the different fraction of these radio pharmaceuticals bound to RBCs (3). This can be explained by the fact that the RBC-bound fractions do not participate in the process of tubular secretion because the diffusion of these agents out of the RBCs into the plasma is very slow (11).

For comparative clearance determination of kit-prepared 99mTc-MAG3 and OH, it is indispensable that preparations with an exact radiochemical definition be used, namely in simultaneous studies. Measurements carried out under steady-state conditions are preferable, however, the minimum requirement using a slope technique is that the clearance calculation be done according to the same model.

REFERENCES


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REPLY: The subject of our article (1) deals with the evaluation of kit prepared MAG3 used for dynamic renal scintigraphy in patients in comparison with our reference substance 123I-hippurate, and it was not a detailed study of the mechanism of the renal clearance of MAG3. For that particular purpose, we have performed different studies published elsewhere (2-4), as pointed out in our discussion.

Our study was a combined study of renal scintigraphy and clearance measurements. A gamma camera cannot distinguish between 123I and 99mTc. Therefore, we had to make the examinations on different days. From a clinical point of view, stable kidney function existed between the two studies. Simultaneous constant infusion, clearance studies using both 123I-hippurate, 51Cr-EDTA, and 99mTc-MAG3, have been used in our earlier experimental studies in rats with results similar to those obtained in our patients and also similar to those published by other authors (5-8).

Our comparative scintigraphic study (1) was based on 17 patients. In a separate paper published recently in the European Journal of Nuclear Medicine (4), we focused only on the clearance of MAG3 and expanded the number of patients and got substantially the same results. These are also in accordance with results of other authors (5-8). Thus, our results seem to be representative. In this context, we want to point out that from an ethical point of view we think it is important to restrict the number of double radionuclide studies to the lowest acceptable level. Our ethical and regional isotope committee uses this restrictive policy. Bubeck and Brandau's argument that "the clearance values
The Difference in Clearance Between Kit-Prepared Technetium-99m-MAG₃ and Radioiodinated Hippuric Acid

Bernd Bubeck and Wolfgang Brandau