were performed during slope with the aid of totally different methods" is an exaggeration. For both ^{123}I-hippurate and for MAG_3 the single-injection plasma clearance method was used. For ^{123}I-hippurate, the one-sample method according to Tauxe (*9*) was used. For MAG_3, the conventional multi-sample method was used. Tauxe's method has been documented extensively, correlates well to the multi-sample technique, and is our routine method for ^{123}I-hippurate.

The radiochemical purity of our MAG_3 kit is specified by the manufacturer to be better than 95% (*10*), and our own measurements using HPLC in 10 preparations showed 97.9% ± 0.9%. These measurements were published in our paper on clearance investigations (*4*). Our papers (*1,4*) deal with the evaluation of a commercial MAG_3 kit. It is clear that for clinical routine use it is not practical to use HPLC-purified MAG_3 as Bubeck et al. (*6*) did in their study.

In our discussion of the renal handling of MAG_3, we refer to our earlier studies using the same kit (*2,3*). In these studies, we used both constant infusion and micropuncture technique on glomerular and different nephron levels. We could show, that both the tubular secretion and the glomerular filtration of MAG_3 were significantly lower than that of ^{125}I-hippurate. This is in contradiction to Bubeck and Brandau's assumption that due to high protein binding the filtration of both MAG_3 and hippurate is "low" which implies the differences to be *insignificant* without any experimental and statistical support. Tubular secretion rate of MAG_3 also has been measured in our micropuncture study (*3*). In our discussion (*1*), we refer to these results. We refer also to other results (*6*), e.g., the lower affinity to the tubular transport system as one possible cause for the decrease in tubular secretion.

Concerning our discussion about whole blood-clearance values in the literature, we wanted to point out in our paper that such measurements do not give sufficient information about the renal handling. The reason is that both blood cell content and the penetration process are included in blood clearances. Since these two parameters are significantly different for MAG_3 and hippurate, as shown in our earlier study (*2*), it is improper to use those values to characterize the renal handling of MAG_3. Bubeck and Brandau claim that the "relation between whole blood clearance of MAG_3 and OIH is higher than the relation between the respective plasma clearance by a factor which can be calculated precisely." This statement is correct, but we do not understand why one should measure this factor precisely (i.e., blood cell activity and plasma activity) in order to determine renal clearance. Blood clearances alone are not, as we and others outline, sufficient for that purpose.

REFERENCES

1. Müller-Suur R, Bois Svensson I, and Mesko L. A comparative study of renal scintigraphy and clearance with technetium-99m- MAG-3 and Iodine-123-hippurate in patients with renal disorders. *J Nucl Med* 1990;31: 1811–1817.
2. Müller-Suur R, Müller-Suur C. Renal and extrarenal handling of a new imaging compound (99m-Tc-MAG-3) in the rat. *Eur J Nucl Med* 1986;12:438–442.
3. Muller-Suur R, Müller-Suur C. Glomerular filtration and tubular secretion of MAG-3 in the rat kidney. *J Nucl Med* 1989;30:1986–1991.
4. Müller-Suur R, Magnusson G, Bois Svensson I and Jansson B. Estimation of technetium-99m mercaptoacetyltriglycine plasma clearance by use of one single plasma sample. *Eur J Nucl Med* 1991;18:28–31.
5. Jafri AR, Britton KE, Nimmon CE. Technetium-99m-MAG3, a comparison with iodine-123 and iodine-131-orthoiodohippurate in patients with renal disorder. *J Nucl Med* 1988;29:147–158.
6. Bubeck B, Brandau W, Steinbaecher M. Technetium-99m labeled renal functioning and imaging agents. *Nucl Med Biol* 1988;15:109–118.
7. Claessens RAMJ, Corstens FHM. Tc-99m-MAG-3 clearance determined in patients by simplified methods. In: Schmidt HAE, Chambron J, eds. *Nuclear medicine*. Stuttgart: Schattauer Verlag; 1990:432–434.
8. Russel CD, Taylor A, Eshima D. Estimation of technetium 99m-MAG-3 plasma clearance in adults from one or two blood samples. *J Nucl Med* 1989;30:1955–1959.
9. Tauxe, WN. Tubular function. In:Tauxe WN and Dubovsky E, eds. *Nuclear medicine in clinical urology and nephrology*. Norwalk: Appleton; 1985:77–105.
10. Ensing GJ, Nielsen J, Panek-Finda H. Development of a kit formulation for the labelling of mercaptoacetyl triglycine (MAG_3) with ^{99m}Tc. *Eur J Nucl Med* 1988;14:303.

R. Müller-Suur
Ingeborg Bois-Svensson
Laszlo Mesko
Danderyds Hospital
Stockholm, Sweden

Prevention of Metoclopramide-Induced Akathisia During Gastric Emptying Imaging.

TO THE EDITOR: During radionuclide gastric emptying (RGE) studies, we sometimes administer the drug metoclopramide (MCP) to hasten gastric emptying in those patients having prolongation of gastric emptying half-time to reveal function or presence of gastric outlet obstruction (*1*). We also have found intervention with MCP to be of considerable value in prediction of its therapeutic efficacy in patients with diabetic gastroparesis (*1*), anorexia nervosa (*2*), or bulimia (*3*). One of us (RWB) has noted akathisia, or motor restlessness, in certain patients receiving the drug at his institution. The response is characterized by an inability of the patient to lie still and the inner need to arise and depart from the imaging bed after injection of MCP. In our experience, older male patients (over age 34 yr) are resistant to akathisia; while females of all ages and younger males are more susceptible. The response occurs after intravenous injection of 10 mg MCP as a bolus over 2–3 min. The onset of restlessness is fairly rapid and usually occurs within 10 min after administration. It has caused premature termination of the imaging study on several occasions. A prospective study at one or our institutions (RMH) over a 7-mo period revealed four akathisic episodes in 20 female patients (20%) and one episode in six male patients (17%).

Akathisia is an important adverse effect of drugs like MCP or antipsychotic medications having dopamine receptor-antagonist activity (*4*). In volunteers, akathisia is described as very common after intravenous MCP but not after oral dosing (*5*).

Management of akathisia is possible. Ratey and Salzman (*6*) report that reduction of dose or elimination of the neuroleptic (antipsychotic) drug is the only truly effective method. However, they found that the beta blockers propranolol and nadolol are somewhat effective. However, the effect of such drugs on RGE is unknown.

Over a decade ago, Bateman et al. (*5*) reported that in normal males receiving oral MCP, akathisia occurred only in subjects who had peak plasma concentrations of drug above 100 ng/ml. That suggested that we should slow the rate of MCP injection. Accordingly, 10 mg of MCP are now added to 50 ml physiologic saline in a flexible bag; the resulting dilution is then infused into the patient intravenously at a rate of 60 drops per min through a heparin lock. To evaluate efficacy of that new dosing technique,

a prospective clinical trial was performed at RMH. From June 1990 through February 1991, a total of 33 patients received MCP for RGE study. There were 23 female patients age 61.7 ± 16.2 yr (mean ± s.d.) with age range 28–87 yr. There were ten male patients of age 54.9 ± 19 yr (age range 14–80 yr). Of those patients, one female subject (age 30 yr, weight 65 kg) reported only, "My head feels numb; I feel strange all over." No treatment of the reaction was instituted, and it spontaneously ended after a few moments. The hospital's adverse reaction committee judged it to be a very mild reaction. No akathisic episode occurred during the trial.

The nuclear medicine clinician and technologist should be aware of this bizarre iatrogenic reaction to MCP and a means for its alleviation, so as to salvage as much diagnostic data from RGE as possible.

REFERENCES

1. Domstad PA, Kim EE, Coupal JJ, et al. Biologic gastric emptying time in diabetic patients, using Tc-99m-labeled resin-oatmeal with and without metoclopramide. *J Nucl Med* 1980;21:1098–1100.
2. Domstad PA, Shih W-J, Humphries L, et al. Radionuclide gastric emptying studies in patients with anorexia nervosa. *J Nucl Med* 1987;28:816–819.
3. Shih W-J, Humphries L, Digenis GA, et al. Tc-99m-labeled triethelene tetraamine polystyrene resin gastric emptying studies in bulimia patients. *Eur J Nucl Med* 1987;13:192–196.
4. Isah AO, Bateman DN. Akathisia and antipsychotic drugs. *Lancet* 1987;i:48.
5. Bateman DN, Kahn C, Davies DS. Concentration effect studies with oral metoclopramide. *Br J Clin Pharmacol* 1979;8:179–182.
6. Ratey JJ, Salzman C. Recognizing and managing akathisia. *Hospital Community Psychiatry* 1984;35:975–977.

Robert W. Beightol
John J. Coupal
Wei-Jen Shih
Roanoke Memorial Hospitals
Roanoke, Virginia
Veterans Affairs Medical Center
Lexington, Kentucky

Serum Thyroglobulin and Whole-Body Iodine-131 Scan in the Management of Differentiated Thyroid Carcinoma

TO THE EDITOR: Ronga et al. (*1*) recently compared serum thyroglobulin (Tg) measurement and ^{131}I whole-body scan (WBS) for the diagnosis of residual tumor or metastases in post-surgical patients with differentiated thyroid carcinoma. It is difficult to understand their assertion that when both tests are considered, both sensitivity and specificity are increased relative to either test considered alone. The process of considering both tests implies defining positivity in one of the two following ways: (a) Tg *and/or* WBS positive or (b) Tg *and* WBS positive. The first definition could increase sensitivity and decrease specificity by adding to the number of true- and false-positives. The effect of the second definition would be the opposite. Logically, neither definition could effect improvement of both sensitivity and specificity.

REFERENCE

1. Ronga G, Fiorentino A, Paserio E, et al. Can iodine-131 whole-body scan be replaced by thyroglobulin measurement in the post-surgical follow-up of differentiated thyroid carcinoma? *J Nucl Med* 1990;31:1766–1771.

Herbert A. Klein
University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania

REPLY: The comment made by Dr. Klein is correct, but it is not appropriate for our study. This is because we took in consideration different criteria in defining positivity for calculation of sensitivity and specificity of thyroglobulin (Tg) and whole-body scan (WBS) alone. As can be seen in Figure 4 of our paper (*1*), we considered Tg capacity to discriminate between the presence of metastases and the presence of residual thyroid tissue; we calculated WBS capacity to distinguish between patients with metastases or residual thyroid tissue and patients with none of them. We appositely made this difference since a WBS, performed soon after surgery, always allows recognition of a residual thyroid tissue from a lymph node or other metastases, whereas the finding of a high Tg value does not allow this discrimination. Moreover, even if we would have taken in consideration the same criteria, when we calculate sensitivity and specificity considering Tg and/or WBS positivity, we would have found an increase in sensitivity but not a decrease in specificity, because the specificity for WBS alone was 100%.

Thus, the simple formula explained by Dr. Klein can be generally applied unless, as in our study, the specificity or the sensitivity of one of the two parameters alone is 100%.

REFERENCE

1. Ronga G, Fiorentino A, Paserio E, et al. Can iodine-131 whole-body scan be replaced by thyroglobulin measurement in the post-surgical follow-up of differentiated thyroid carcinoma? *J Nucl Med* 1990;31:1766–1771.

Giuseppe Ronga
Alberto Signore
II Clinica Medica
Rome, Italy