epidermoid carcinoma have shown increased local activity thought to be due to local marrow hyperplasia (*1,8*). There is one reported study which revealed mild to moderate [^{111}In] WBC uptake in some noninfected closed fractures (*11*). However there are no reported cases of uptake of the magnitude we describe. A mechanism for this phenomenon has not been reported. Proposed explanations include persistent inflammation around fracture site or less likely in our patient hemorrhage (since there was no evidence of thrombus in this case). Since many patients with severe trauma develop fever, radiologists should be aware of the possibility that there may be increased activity present in simple fracture sites, and thus avoid costly unnecessary tests.

References

1. McAfee JG, Samin A. In-111 labeled leukocytes: a review of problems in image interpretation. *Radiology* 1985; 155:221–229.
2. Schauwecker DS, Park H-M, Mock BM, et al. Evaluation of complicating osteomyelitis with Tc-99m MDP, In-111 granulocytes, and Ga-67 citrate. *J Nucl Med* 1984; 25:849–853.
3. Propst-Proctor SL, Dillingham MF, McDougall IR, et al. The white blood cell scan in orthopedics. *Clin Ortho Rel Res*, 1982; 168:157–165.
4. Wing VW, van Sonnenberg E, Kipper S, et al. Indium-111 labeled leukocyte localization in hematomas: a pitfall in abscess detection. *Radiology* 1984; 152:173–176.
5. Fernandez M, Stern PJ, Volarich JC, et al. Evaluations of In-111 white blood cells in the detection of skeletal disease. *J Nucl Med* 1982; 23:29.
6. D'Alonzo WA, Alavi A. Detection of deep venous thrombosis by indium-111 leukocyte scintigraphy. *J Nucl Med* 1986; 27:631–633.
7. Segal AW, Arnot RN, Thakur ML, et al. Indium-111-labeled leukocytes for localization of abscesses. *Lancet* 1976; 2:1056–1058.
8. Sfakianakis GN, Mnaymneh W, Ghandur-Mnaymneh L, et al. Positive Indium-111 leukocyte scintigraphy in a skeletal metastasis. *Am J Roengenol* 1982; 139:601–603.
9. Coleman RE, Welch D. Possible pitfalls with clinical imaging of indium-111 leukocytes: concise communication. *J Nucl Med* 1980; 21:122–125.
10. Sfakianakis GN, Al-Shekhw, Neal A, et al. Comparisons of scintigraphy with In-111 leukocytes and Ga-67 in the diagnosis of occult sepsis. *J Nucl Med* 1982; 23:618–626.
11. Abreu SH, Van Nostrand D, Lower R, et al. Indium-111 labeled white blood cell (In-WBC) uptake in non-infected closed fractures in humans: a prospective study. *J Nucl Med* 1987; 28:586.

Frank Callcott
Leonie Gordon
Stephen I. Schabel
Richard Friedman
Medical University of South Carolina
Charleston, South Carolina

Radiochemical Purity of [^{99m}Tc]HM-PAO

TO THE EDITOR: Technetium-99m d,l-hexamethyl propyleneamine oxime ([^{99m}Tc]HM-PAO) is an exciting new radiopharmaceutical which permits SPECT imaging of regional cerebral perfusion with the convenience of a technetium kit. It was approved for general use in Canada in November, 1986 (Ceretec, Amersham Canada, Ltd.)

Addition of pertechnetate to a freeze-dried HM-PAO kit produces a mixture of radiochemical species which changes with time. In addition to the desired lipophilic [^{99m}Tc]HM-PAO complex, there are free pertechnetate, reduced-hydrolyzed technetium, and an unidentified secondary complex which is less lipophilic than [^{99m}Tc]HM-PAO (*1*). The relative amounts of these components are influenced by the "quality" of pertechnetate used in preparation (time since elution and amount of carrier ^{99}Tc) and the time after reconstitution of the kit. It is recommended that the pertechnetate be eluted <4 hr previously from a generator with no more than 24 hr of in-growth and that the radiopharmaceutical be injected within 30 min of reconstitution (*1,2*). These constraints emphasize the importance of determining the radiochemical purity of [^{99m}Tc]HM-PAO. Furthermore, determination of the amount of lipophilic [^{99m}Tc]HM-PAO present will be required for mathematical modelling of HM-PAO kinetics and quantification of regional cerebral perfusion.

Neirinckx and others (*1*) present a chromatographic procedure which uses paper and instant thin-layer strips in three solvent systems to determine the amounts of the three impurities and then the amount of the desired complex by difference. This seemingly complex procedure results in many users neglecting quality control completely. It consumes much of the 30-min shelf-life of the radiopharmaceutical. In addition, we have obtained anomalous results ~15% of the time.

We would like to propose the following simpler, more rapid procedure for routine quality control of [^{99m}Tc]HM-PAO. Several drops of the radiopharmaceutical are added to a test tube which contains 3 ml ethyl acetate and 3 ml saline. The tube is capped, mixed on a vortex mixer for 1 min, then allowed to stand for 1 min to let the phases separate. The top layer (ethyl acetate) is transferred by pipet to another tube and the activities in each layer are measured in a dose calibrator. The fraction present as lipophilic [^{99m}Tc]HM-PAO is calculated as the activity in the top layer divided by the total activity in the two layers. The lipophilic [^{99m}Tc]HM-PAO is extracted into ethyl acetate while free pertechnetate, reduced-hydrolyzed technetium, and the secondary complex remain in the aqueous layer.

Comparison of the results of the extraction and three-system chromatographic methods produced a regression line with a slope of 1.02, an intercept of 3.2%, and a correlation coefficient of 0.985 ($p < 0.001$) for 24 measurements. The coefficient of variation was 1.2% for the extraction method and 3.2% for the chromatographic method. Ethyl acetate was selected because it is easier to handle than diethyl ether and phase separation is more rapid than with octanol. Chloroform produced equivalent results.

A similar approach to direct quantification of the lipophilic complex has been suggested by the Missouri group (*3*) who used paper chromatography with diethyl ether as solvent, but this is not as rapid as the extraction method. An alternative to solvent extraction might be the use of an extraction cartridge (C-18 SEP-PAK, Waters Associates), which would be even more rapid but also more expensive.

In conclusion, we suggest that the radiochemical purity of [^{99m}Tc]HM-PAO be routinely checked with an extraction procedure which requires <5 min to complete, can be per-

formed in any department, and provides a direct measure of lipophilic [^{99m}Tc]HM-PAO. This method produces comparable results to the three-system chromatographic procedure and is less variable.

References

1. Neirinckx RD, Canning LR, Piper IM, et al. Technetium-99m d,l-HM-PAO: a new radiopharmaceutical for SPECT imaging of regional cerebral perfusion. *J Nucl Med* 1987; 28:191–202.
2. HM-PAO package insert. Amersham Canada Ltd., 1986.
3. Hung CY, Volkert WA, Holmes RA: A kinetic analysis of Tc-99m-d,l-HM-PAO: decomposition in aqueous media [Abstract]. *J Nucl Med* 1987; 28:593.

James R. Ballinger
Robert H. Reid
Karen Y. Gulenchyn
Ottawa, Civic Hospital
Ottawa, Ontario, Canada

Gender-Related Differences in Gastric Emptying

TO THE EDITOR: We have read with interest the article by Datz et al. (*1*) on gender-related differences in gastric emptying (GE). Their data, in fact, coincides with studies we published several years ago (*2,3*), despite variations in the method; as is usual among groups who investigate GE. The magnitude of the difference between males and females found by Datz, expressed in terms of T1/2 is almost identical to that we described (*3*); T1/2 is 1.4 to 1.5 times more prolonged in females than in males. These results are also similar to those reported recently by Hutson et al. (*4*).

In our work (*3*) we studied 18 women, the ages ranged from 18 to 27 yr, with a mean of 23 yr, who did not take contraceptives for the previous 6 mo, and all the studies were performed in the afternoon. We found a relationship between GE and the phase of the menstrual cycle, with a significant tendency to a faster GE in the ovular phase. There was no difference between the follicular and luteal phases. This finding has not been confirmed by Horowitz et al. (*5*), studying ten women with a wider age range (from 26 to 45 yr, with a mean of 36 yr), who had bilateral ovarian tubal ligation performed from 6 to 120 mo previously. All the studies were performed in the morning. In this study no differences was noted between the follicular and luteal phases, but the ovular period was not studied. However, there is a previous observation by McDonald (*6*) who described a faster GE of a liquid meal during ovulation.

Unfortunately, in their study of 15 women aged from 23 to 44 yr, with a mean of 32 yr, Datz et al. do not inform us of the phase of the subjects' menstrual cycle. The day of the menstrual cycle on which GE studies were done is necessary to ascertain the importance of a progesterone effect on GE.

Since circadian variations in GE have been observed (*7*), the time of the day in which the studies were performed is also relevant. Other facts that can influence GE and should be mentioned are: dietary habits of the population studied (*8*), fast duration (*9*), degree of physical activity (*10*), and smoking habit (*11*).

Early studies to investigate possible differences in GE between sexes probably failed due to technical insufficiencies, for example, fractionate liquid aspiration at 10 and 20 min only (*12*). There are, however, several clinical facts in gastrointestinal pathology which suggest a hormonal influence on gastrointestinal motility, e.g., the apparition of gastroesophageal reflux and biliary ectasis during pregnancy. Furthermore, sexual receptors in the stomach and gastrointestinal tract of the baboon and cobaya have been recently identified (*13,14*).

We agree with Datz et al. in the sense that differences in GE between sexes are due to an effect of sex hormones on gastrointestinal motility. We believe that further studies are required to ascertain the influence of the phase of the menstrual cycle, and probably of the hormonal situation related to age, on gastric motility.

The exact adjustment to a monoexponential pattern in GE of liquids is still controversial. GE of liquids is often considered only to approximate an exponential model (*15*). In our study (*3*), such an exact adjustment to a monoexponential pattern was only possible in nine of 50 cases; in the remaining there was a better fit to a biphasic model, with a faster first phase followed by a stationary phase. This finding has also been described by other authors (*16*), and seems in agreement with the effect of gravity after ingestion (described by Hunt), with the passive escape of liquids to the duodenum before mixing with solids (*17*), and with the noninitiation of the gastric reflex of receptive relaxation when ingestion is <1 kg (*18*).

GE studies using radiolabeled test meals have contributed to the knowledge of the diversity of factors that influence gastric motility. We believe that with caution when deriving conclusions, radionuclide GE studies can still offer significant contributions to gastroenterology.

References

1. Datz FL, Christian PE, Moore J. Gender-related differences in gastric emptying. *J Nucl Med* 1987; 28:1204–1207.
2. Notivol R, Carrió I, Vilardell F. Some observations on gastric emptying. *Hepatogastroenterology* 1983; Vol 30, 2:76.
3. Notivol R, Carrió I, Cano L, et al. Gastric emptying of solid and liquid meals in healthy young subjects. *Scand J Gastroenterol* 1984; 19:1107–1113.
4. Hutson W, Roehrkasse R, Kaslewicz F, et al. Influence of sex and weight on gastric emptying. *Gastroenterology* 1987; 92:1443.
5. Horowitz M, Maddern GJ, Chatterton BE, et al. The normal menstrual cycle has no effect on gastric emptying. *Br J Obstet Gynaecol* 1985; 92:743–746.
6. McDonald I. Gastric activity during the menstrual cycle. *Gastroenterology* 1957; 30:602–607.
7. Goo RH, Moore JG, Greenberg E, et al. Circadian variation in gastric emptying of meals in man. *Gastroenterology* 1987; 92:1408.
8. Hunt JN. A possible relation between the regulation of gastric emptying and food intake. *Am J Physiol* 1980; 2:1–4.
9. Evans D, Foster G, Hardcastle J. Disruption of the human migrating motor complex by meals of varying calorific values. *Gut* 1983; 24:A-471.
10. Carrió I, Estorch M, Serra-Grima R, et al. Gastric emptying and exercise. A method to assess the influence of physical training on gastric motility. *Nucl Med* 1987; 26:79–80.