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## Radiochemical Purity of Technetium-99m-HMPAO Depends on Specific Activity

**TO THE EDITOR:** Radiochemical purity (RCP) quality control is routinely carried out before administering $^{99m}$Tc-HMPAO. After following kit instructions for labeling (*1*), we observed a low RCP related to the use of pertechnetate eluates obtained approximately 24 hr after the previous elution (generator in-growth 24 hr). We suspected that the technetium used was not of sufficient quality due to radiolysis or an excess of $^{99}$Tc (i.e., low-specific activity $^{99m}$Tc), so we decided to use only the second eluates obtained within 1–4 hr after the previous elution (generator in-growth 1–4 hr).

Quality control of RCP was carried out using the method of extraction with chloroform by Ballinguer (*2*). The correlation obtained from a study carried out previously in our laboratory when this method was compared with the chromatographic method of Neirinkx (*3*) was:

$$y\ (\text{Chromatographic Method}) = 0.909\ x\ (\text{Extraction Method}) + 6.36, \quad \text{Eq. 1}$$

where $r = 0.986$, $p < 10^{-6}$, and $n = 27$.

Labeling carried out with technetium obtained with a generator in-growth 24 hr (22.6 ± 2.6) gave:

$$RCP = 85.2\% \pm 16.4\%\ (n = 42). \quad \text{Eq. 2}$$

In 15 preparations, the RCP was <90% and in 10 preparations <80% (Table 1). The results were analyzed for the effect of total amount of radioactivity. No statistical significant difference in RCP was found between both groups.

Labeling with technetium obtained with a generator in-growth 1–4 hr (2.5 ± 0.7) gave:

$$RCP = 93.9\% \pm 1.6\%\ (n = 181). \quad \text{Eq. 3}$$

Only one preparation resulted in a RCP <90%. Table 2 shows various preparations according to the radioactivity used for labeling.

**TABLE 1**
RCP for Two Pertechnetate Eluates

| Activity (MBq) | Generator in-growth (hr) | RCP % | n |
|---|---|---|---|
| 1087 ± 159 | 23.9 ± 2.1 | 83.3 ± 18.4 | 22 |
| 2723 ± 533 | 22.6 ± 2.5 | 87.3 ± 13.7 | 20 |

**TABLE 2**
Various Pertechnetate Preparations

| Activity (MBq) | RCP % | n |
|---|---|---|
| 1591 ± 222 | 92.0% ± 1.4 | 5 |
| 2216 ± 44 | 93.6% ± 1.5 | 94 |
| 2941 ± 78 | 94.3% ± 1.4 | 77 |
| 3626 ± 148 | 94.0% ± 1.8 | 5 |

To obtain high RCP with $^{99m}$Tc-HMPAO, an elution obtained a few hours after the previous elution (within 1–4 hr) should be used. This permits an increase of radioactivity labeling to at least 3000 MBq. Furthermore, this would represent a considerable economic saving since it would result in several doses from a single vial.

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## Renal Clearance of Technetium-99m-MAG3: Normal Values

**TO THE EDITOR:** We are frequently asked about normal values for $^{99m}$Tc-MAG3 clearance. Technetium-99m-MAG3 has become the renal agent of choice in many clinical contexts. Its clearance, easily calculated from a single timed blood sample, can be used directly as a measure of renal function and can also be converted to effective renal plasma flow (ERPF) by applying a correction factor (*1*).

When $^{99m}$Tc-MAG3 clearance ($C_{MAG3}$) is converted to ERPF (or $C_{PAH}$), conventional normal values for ERPF can be employed, such as the normal values obtained at this center from OIH clearance ($C_{OIH}$) in a series of normal transplant donors (*2*). Since renal donors have such extensive presurgical evaluation, they constitute a normal reference population in which renal disease has been truly ruled out.

We now have accumulated enough experience with $^{99m}$Tc-MAG3 in transplant donors to report normal values measured directly with $^{99m}$Tc-MAG3 rather than with OIH. Data from 200 donors were reviewed (86 male, 114 female, ranging in age from 20 to 66 yr). $C_{MAG3}$ was calculated from a single 45-min blood sample by two methods (*3–5*) and ERPF was estimated by a third method (*6*). Normal values are reported for each method.

At our clinic, ERPF has been measured routinely for many years with the Tauxe one-sample method using $^{131}$I-OIH. The Tauxe ERPF formula yields values about 10% higher than true $C_{OIH}$ (*1*), compensating for the difference between $C_{OIH}$ and $C_{PAH}$ (*7*). When we switched from OIH to $^{99m}$Tc-MAG3, we

continued to report an ERPF estimate, making use of the strong empirical correlation between $C_{MAG3}$ and $C_{OIH}$. Using that method (*6*), the ERPF measured in the 200 transplant donors and scaled for body surface area was found to be:

$$ERPF = 568 \pm 126 \text{ for age} < 40,$$

$$ERPF = 568 - 5.83(A - 40) \pm 126 \text{ for age } A \geq 40.$$

The mean and standard deviations are given in ml/min/1.73 $m^2$, i.e., scaled to standard adult surface area.

The data are plotted in Figure 1. Comparison of these data with the normal values published by Tauxe (*2*) shows little difference, as would be expected, since the $^{99m}$Tc-MAG3 method was deliberately constructed to agree with the OIH results. One can thus estimate ERPF from $C_{MAG3}$ and interpret the results using standard normal values from the literature.

Formulas for calculating $C_{MAG3}$ (which is only 59% of $C_{OIH}$ or 53% of ERPF) have been published by Russell (*3*) and by Bubeck (*4,5*). Using those formulas, the normal values for the Russell formula become:

$$C_{MAG3} = 304 \pm 70 \text{ for age} < 40,$$

$$C_{MAG3} = 304 - 3.27(A - 40) \pm 70 \text{ for age } A \geq 40,$$

and for the Bubeck formula:

$$C_{MAG3} = 263 \pm 44 \text{ for age} < 40,$$

$$C_{MAG3} = 263 - 2.34(A - 40) \pm 48 \text{ for age } A \geq 40.$$

The mean and standard deviations are given in ml/min/1.73 $m^2$, i.e., scaled to a standard adult surface area.

The Bubeck formula gives lower values than the Russell formula when $C_{MAG3}$ is in the high normal range (Fig. 2). This difference is not apt to be of clinical consequence, as long as the two methods are not indiscriminately mixed, but it leads to a difference in the normal values.

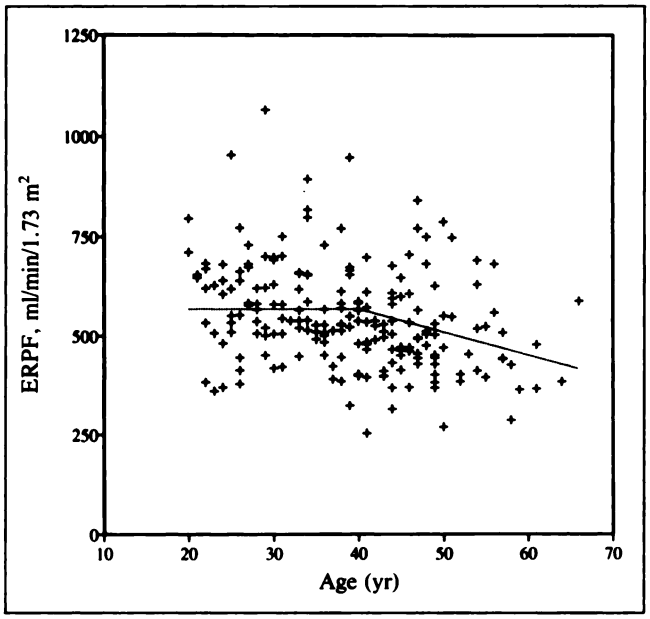


**FIGURE 1.** Single-sample ERPF (ml/min/1.73 $m^2$) in normal transplant donors versus age of donor.

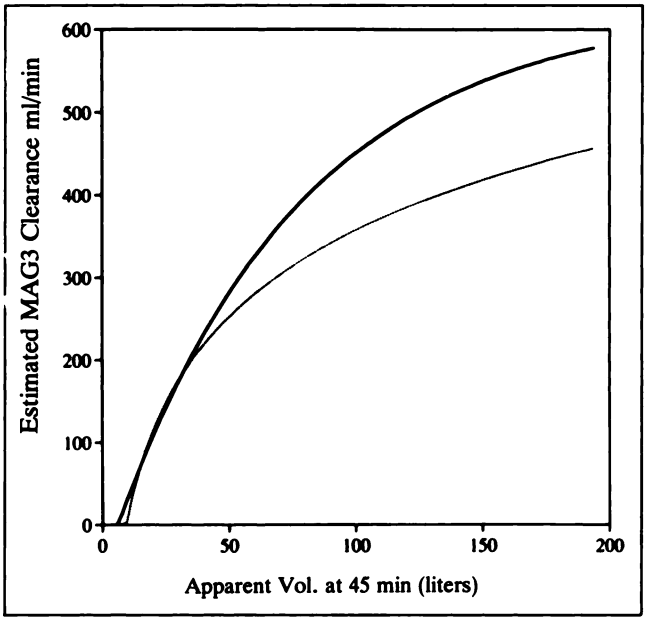


**FIGURE 2.** $C_{MAG3}$ (ml/min) versus apparent distribution volume in liters at 45 min (i.e., reciprocal of 45-min plasma concentration measured in fraction of administered dose per liter) for a subject who is 170 cm tall and weighs 70 kg. Solid line is the Russell formula (*3*). Dotted line is the Bubeck formula (*4,5*).

When using the Russell formula, $C_{MAG3}$ can be converted to ERPF by dividing by 0.53, with results in close agreement with the widely used Tauxe formula for OIH (*8*). The factor of 0.53 results from the fact that $^{99m}$Tc-MAG3 clearance is 59% of $C_{OIH}$, (*1*) which in turn is 90% of $C_{PAH}$ (*7*). We used the measurements interchangeably with the conversions as follows:

$$C_{MAG3} = 0.59\ C_{OIH} = 0.53\ C_{PAH},$$

$$C_{OIH} = 0.90\ C_{PAH},$$

$$ERPF = C_{PAH}.$$

In our experience, the best use of a reliable quantitative measurement of renal function is not simply to separate normal from abnormal, but rather to monitor changes in renal function on serial studies. For this reason, the normal value is seldom very important.

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## Radiolabeled Immunoglobulin Scintigraphy for the Diagnosis of Spondylodiscitis

**TO THE EDITOR:** Datz et al.'s article on the efficacy of $^{111}$In-polyclonal immunoglobulinG (IgG) to detect infection and inflammation (*1*) contains one case of spondylodiscitis in which scintigraphy with $^{111}$In-IgG yielded a positive result. Another five true-positive results have been obtained with this tracer in cases of spondylodiscitis caused by various organisms (*2*).

Labeled leukocytes have difficulty establishing the diagnosis of spondylitis/spondylodiscitis (*3–5*). Uptake of $^{67}$Ga is aspecific. Therefore, polyclonal IgG potentially could be useful for this diagnosis. However, since no other spinal diseases have been included in the above mentioned series, questions about the specifity of this method for the diagnosis of spondylodiscitis still need to be addressed.

Results obtained with $^{99m}$Tc-IgG have been less encouraging. In one study using iminothiolane-derived IgG, three cases of spondylitis were found false-negative with $^{99m}$Tc-IgG (*6*). Another study using DTPA conjugated IgG, reported one false-negative and two true-positive results (*7*). Our own experience with $^{99m}$Tc-IgG for the diagnosis of spondylodiscitis is summarized in Table 1. Images were obtained at approximately 5 and 24 hr after injection of 555 MBq $^{99m}$Tc-IgG labeled via its iminothiolane derivative.

From these cumulative data, it would appear that $^{99m}$Tc-IgG lacks sensitivity for the diagnosis of spondylodiscitis, perhaps unlike its $^{111}$In-labeled counterpart. Differences between the biodistribution of $^{111}$In- and $^{99m}$Tc-IgG have also been observed in animal models of focal infection (*8*). Technetium-IgG radiolabeled via the hydrazino nicotinamide derivative is known from animal studies to behave more like $^{111}$In-IgG (*9*).

In conclusion, although radiolabeled IgG may hold promise for the diagnosis of infectious spondylitis, further studies in more extensive patient groups are required to define its specificity and sensitivity in this respect, as well as the radiolabel and radiolabeling method of choice.

**TABLE 1**
**Technetium-99m-IgG Imaging in Six Patients with Suspected Spondylodiscitis**

| Sex | Age | Location | Verification procedure | Imaging |
|---|---|---|---|---|
| M | 77 | L4–L5 | CT, MRI, culture (*Candida parapsilosis*) | TP* |
| F | 47 | L1L2 | CT, MRI | FN |
| M | 47 | L4L5 | Ziehl staining of surgical specimen | FN |
| F | 32 | L3L4, L4–L5 | Follow-up | TN† |
| F | 41 | L5S1 | MRI | TN |
| F | 24 | Lumbar spine | Follow-up | TN |

*Abscess with extravertebral extension.
†Previous spondylodiscitis due to *Pseudomonas aeruginosa*.
TP = true-positive; FN = false-negative, TN = true-negative.

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**REPLY:** There are a number of problems with using radionuclide infection imaging agents for diagnosing osteomyelitis/discitis of the spine, especially in postoperative patients.

Indium-111-leukocytes detect most musculoskeletal infections with reported sensitivities ranging from 83% to 100%. Several recent studies, however, have shown that $^{111}$In-leukocytes are less sensitive for spine infections. In 22 patients with biopsy proven osteomyelitis/discitis, Whalen et al. found that the leukocyte scan had a sensitivity of only 13% (*2*). Palestro et al. studied 71 patients with suspected vertebral osteomyelitis and found only 39% had increased activity. A total of 7% had normal studies and 54% had photopenic defects (*3*). Unfortunately, photopenia on leukocyte scans is not specific for osteomyelitis. Cold defects have been described in tumor, radiation, fracture, Paget's disease, degenerative arthritis and following surgery (*4*).

It is unclear why labeled leukocytes do not detect vertebral infections as well as other musculoskeletal infections. A pathophysiologic explanation has been offered by Palestro (*5*). Vertebral osteomyelitis likely originates as a septic embolism that lodges in a metaphyseal artery. Retrograde propagation into the metaphyseal anastomosis circumferentially around the vertebral body may involve other metaphyseal arteries, with the development of sequential septic infarcts. Occlusion of such a large number of vessels may impede white cell migration to the site of infection. Lower sensitivity in spine infections may be partially explained by the difficulty in detecting cold defects compared to hot lesions. The timing of the scan may also be important. At the