Eterović, we feel that the excellent correlations observed in our clinical data are prima facie evidence that our assumptions and simplifications are reasonable. In fact, we explicitly correct two terms in Eq. (1) (*1*), errors in which are neglected by many authors. First, calculation of total blood volume from peripheral hematocrit and a RISA plasma volume overestimates TBV by ~ 13% (*6*); we adjust the red cell volume by using a factor of 0.87 to account for the difference between peripheral and central hematocrit. Second, we correct LV parameters for bolus smearing; in nonregurgitant patients the average bolus smearing is ~ 12% (*1*) and its effect is to increase the area under the indicator dilution curve by that amount. Although the errors are roughly offsetting, they are errors nonetheless and should be taken into account explicitly, as we do.

We have found calculation of regurgitant fraction from the stroke counts obtained from a gated equilibrium study to be fraught with difficulty (e.g., selection of background areas, overlapping of heart chambers). Convolution analysis and factor analysis have been proposed and have not achieved widespread acceptance. We feel that first-pass techniques are the only reliable method currently available.

The comments by Eterović regarding shunts are interesting but are relevant to our paper only insofar as shunts and regurgitation are examples of "early" and "instant" recirculation, respectively (*2*).

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Role of Technetium-99m Phosphonate Bone and Indium-111 Leukocyte Scanning for Detecting the Infected Hip Prosthesis

TO THE EDITOR: A recent report by Johnson et al. described the use of technetium-99m (^{99m}Tc) hydroxymethylene diphosphonate (HDP) bone scanning and indium-111 (^{111}In) labeled leukocyte scanning (ILLS) for detecting infected joint prostheses (*1*). They found an increased specificity and accuracy for the two types of scan taken in sequence compared to ILLS alone. Although their study included 21 total hip arthroplasties, the authors made no reference to our report of 50 painful prosthetic hip joints investigated with a [^{99m}Tc]methylene diphosphonate (MDP) bone scan and an ILLS, 32 of whom also had a gallium-67 (^{67}Ga) citrate scan (*2*).

In our study, [^{99m}Tc]MDP bone scans were classified into the following distributions of radioactivity around the prosthesis: normal uptake, focally abnormal uptake, diffusely abnormal uptake, and focal superimposed on diffusely abnormal uptake (the captions to Figure 1 (c) and (d) in Ref. (2) should be interchanged). We classified ILLS and ^{67}Ga scans as abnormal if they demonstrated hyperactivity in any distribution (i.e., by the first of the two ways described by Johnson et al.). Infection was absent in all cases of normal and focal uptake in the [^{99m}Tc]MDP bone scans, and was present in five out of six cases of diffuse uptake. The false-positive diffuse uptake occurred in a case of nonseptic synovitis which also produced a false-positive ILLS. In the 26 prosthetic hips which had focal superimposed on diffuse uptake, infection was present in six cases. Thus for the normal, focal, and diffuse types of ^{99m}Tc uptake, the ILLS was unnecessary. Consequently, the policy in this department is to conduct a [^{99m}Tc]MDP bone scan first and proceed to an ILLS only if the uptake in the former is classified as focal superimposed on diffuse.

Subsequent to conducting our review and before implementing the above policy, we obtained follow-up on a further 11 painful prosthetic hips imaged with [^{99m}Tc]MDP and [^{111}In] leukocytes that endorsed our earlier conclusions. Focal superimposed on diffuse ^{99m}Tc uptake was produced in seven cases. There were two cases of proven infection which were the only cases with diffuse ^{99m}Tc uptake and the only cases with an abnormal ILLS. For completeness, these results have been added to those already published (*2*) and the combined data are given in Table 1.

The implication of Johnson et al.'s study is that all patients investigated for a painful prosthetic hip require an ILLS. If the ^{99m}Tc bone scan is performed first and classified as above, it is our experience that only about half of the patients referred routinely for investigation will require a subsequent ILLS (Table 1). The costly and time-consuming procedure of labeling leukocytes with ^{111}In can be avoided for the remainder.

Applying our method to the two prosthetic hip cases illustrated by Johnson et al., the [^{99m}Tc]HDP bone scan given in their Figure 1 would be classified as focally abnormal and interpreted as uninfected, an ILLS would not have been performed, and the result agrees with their clinical finding of negative for infection by intraoperative cultures. The uptake in the [^{99m}Tc]HDP bone scan shown in their Figure 2 would be classified as diffusely abnormal which would be interpreted as infected, an ILLS would not have been performed, and the result again would agree with their clinical finding of positive for infection by intraoperative cultures.

TABLE 1
Combined Results from Ref. (2) and the Review of 11 Further Cases of [^{99m}Tc]MDP for Detecting Infection Around a Hip Prosthesis

[^{99m}Tc]MDP bone scan uptake	With infection	Without infection
Normal	0	3
Focal	0	17
Diffuse	7	1
Focal + diffuse	6	27

Johnson et al. suggested that the labeling technique and the use of crude rather than pure granulocytes may account for their results being better than those of McKillop et al. (*3*). However, in a study of chronic soft-tissue infection, acute soft-tissue infection, chronic osteomyelitis, and acute osteomyelitis, Schauwecker et al. showed that there was no difference between purified ^{111}In granulocytes and mixed ^{111}In leukocytes (*4*). Chronic osteomyelitis is characterized by a lower granulocyte infiltration than acute osteomyelitis. Infection around some prosthetic joints is associated with a very low grade inflammatory response and may not be obvious to the surgeon at operation, confirmation being obtained from culture of tissue samples. In these circumstances, a false-negative rate with ILLS is to be expected, regardless of the labeling technique (*5*). Variations between the results of different studies are more likely to be a result of this range in inflammatory response and granulocyte infiltration, particularly as the number of infected cases per study is small.

In conclusion, although the ILLS results of Johnson et al. are similar to our own, we recommend that (a) an ILLS is unnecessary for all prosthetic hip referrals: a ^{99m}Tc bone scan should be performed first and an ILLS need only be performed where the ^{99m}Tc uptake can be described as focal superimposed on diffuse, and (b) the ILLS need only be interpreted by the simpler (i.e., the first) method described by Johnson et al.

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REPLY: We reviewed with interest the article by Mountford et al. where the authors classified bone scintigraphy of failed hip prosthesis into normal uptake, focal abnormality, diffusely abnormal, and focally abnormal superimposed on diffusely abnormal (*1*). None of the patients studied in our series with a painful prosthesis associated with x-ray findings of loosened prosthesis exhibited normal activity on bone scan. In fact, it would be most unusual for patients with a radiographically loosened prosthesis not to demonstrate localized areas of increased activity on bone scan secondary to focal areas of abnormal stress transfer from the loosened prosthesis.

We were surprised to read that Mountford et al. advised that patients with a focal abnormality on bone scan and a loosened hip prosthesis need not be investigated any further for infection, since numerous investigators have noted that a wide overlap exists between the focal scintigraphic findings on bone scan secondary to loosening and infection. Furthermore, Mountford et al. made this statement on the basis of only 17 patients in their series with focal abnormality on bone scan and no evidence of infection. This is an extraordinarily strong statement to make as the pertinent literature over the past two decades continues to find this a somewhat controversial issue.

We would also like to stress a word of caution with respect to the statement by Mountford et al. when they "classified ILLS and Ga-67 scans as abnormal if they demonstrated hyperactivity in any distribution" (*1*). The reason for this is that gallium-67 or indium-111 white blood cell uptake is not specific for infection in a loosened prosthesis and may be positive even in the absence of culture proven infection in patients with a painful loose hip prosthesis (*2*).

In the reports published by Schauwecker et al., it was demonstrated that there is no statistical difference in sensitivity with mixed leukocyte preparations (MIX) versus pure granulocyte preparations (GRAN). It was also demonstrated, contrary to Mountford's supposition, that there is no statistical difference in the sensitivity of MIX or GRAN preparations in the detection of acute (MIX-88%/GRAN-100%) versus chronic (MIX-83%/GRAN-79%) osteomyelitis. We also feel, from many years experience, that labeling technique has an enormous impact on clinical results. Leukocyte preparations, MIX or GRAN, if produced using poor technique can result in damaged cells and false negative findings. The only method to properly ascertain viability of labeled leukocytes is radiochemotaxis using a modified Boyden chamber (*3,4*). Since the above-mentioned publications made no reference to viability using a standardized technique such as radiochemotaxis, direct comparison of labeling technique is not possible.

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