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REPLY: This statement is based on a fundamental misunderstanding: Peters and colleagues relate the plasma-protein binding of ^{99m}Tc-MAG_3 (reported by us to amount to 90%) to the total plasma volume of ~3 liters (i.e., 2.7 liters), whereas the term "plasma-protein binding" actually indicates the percentage of a substance in the plasma (=100%) bound to plasma proteins. Since 1 liter of plasma contains about 70 g of protein, this means that 90% of ^{99m}Tc-MAG_3 is bound to 210 g of protein and the remaining 10% are distributed "freely" in the plasma water. All data referring to the protein binding in plasma (*1–4*) are related exclusively to the intravascular space and estimations of the relative concentration of this substance in the remaining extracellular fluid can only be made if the measurement was performed under steady-state conditions, which was not the case.

The objection that the value we found was too high due to the fact that it was determined in vitro and thus could be overestimated according to the results of Jeghers et al. (*5*) does not apply. From an objective point of view, that publication (*5*) has been quoted incorrectly. Jeghers et al. have rightly drawn attention to the problem of precipitation reactions as well as to the protein fractions used in vitro, both of which can lead to incorrect results. In the same paper, however, Jeghers et al. demonstrated that there is a very good correlation of ultrafiltration measurements (three working groups, two methods, 85%–91%), a technique accepted by renal physiologists for many years (*6*). Moreover, we used patients' plasma for our measurements so that we had the complete range of proteins in the plasma and thus virtually performed in vivo investigations. The differences in pressure (≤5 bar) during the measurement procedure, as compared to the in vivo situation, have no effect on the degree of protein binding in plasma, since neither a covalent, nor an ionic, nor a Van-der-Waals interaction can be drastically influenced by physical factors of this type. However, it is definitely not possible to calculate the plasma-protein binding of an agent on the basis of the theoretical volume of distribution as Peters et al. have done.

In our study (*1*) although there may exist more realistic models (e.g., *7*), we applied the two-compartment model according to Sapirstein (*8*) to compare our results with regard to clearances, distribution volumes, and biologic half-lives to the results obtained by other authors (*2–4*). Our intention was not the calculation of "real" volumes of distribution, considering that this term has a different definition in each model and is, for instance, also used to describe the reciprocal value of a specific plasma concentration (*9*). What they have in common is that they are theoretical volumes of distribution that cannot be attributed to a true anatomic space, which is also stated by Sapirstein et al. (*8*). As found by Taylor et al. (*2*), we also were able to show (*1*) that according to the two-compartment model the biologic half-lives of orthoiodohippuric acid (OIH) and ^{99m}Tc-MAG_3 are identical in the respective compartments and that the volume of distribution of OIH is higher than that of ^{99m}Tc-MAG_3 by a factor of about 1.5 (on the basis of simultaneous plasma measurements). This results in a lower clearance of ^{99m}Tc-MAG_3 by the same factor as compared to OIH. We succeeded in confirming this theoretical assumption by simultaneous steady-state clearance measurements (*1*). The absolute values for the distribution volumes and for the clearances determined according to the model by Sapirstein do not, however, have to be identical for the different working groups, since they depend, among other factors, on the period of time during which blood sampling was performed.

In our opinion, it is not possible to calculate a "true" volume of distribution, especially during slope; these values mainly serve as a means to compare different substances and to compare relative results obtained with those of other authors using the same model.

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