Plasma Volume Determinations after 20 Years

Plasma volume has been measured clinically with a radionuclide-labeled human serum albumin for about 20 years. Although a number of different radionuclides have been used, as well as a number of labeling methods, the continuum of effort in this area is testimony that radiopharmaceuticals and methods for the determination of plasma volume still do not meet the exacting standards desired for accuracy, ease of preparation, or physical characteristics.

In this issue of the *Journal*, Yang at al. (*1*) have compared plasma volume determinations obtained with both iodine-and technetium-labeled human serum albumin and found a high degree of correlation between the two. In the evaluation of any new procedure, its characteristics and the results obtained must be compared with an established standard. The authors have done this using radioiodinated albumin as the basis for comparison. Their results indicate that human serum albumin labeled with technetium provides data as accurate as that obtained with the standard iodinated label. At face value this suggests that the technetium-labeled product would be preferable because it offers reduced radiation exposure to the patient, permits repeat plasma volume determinations more readily, and does not sacrifice accuracy.

The authors evaluated a commercially available human serum albumin kit that uses stannous tartrate as the reducing agent for labeling with technetium. To determine the dilution of the administered labeled HSA, an aliquot of the originally prepared material is used as the standard, and the measurement of this standard reflects the total radioactivity per unit volume in the original material. By sequential sampling of venous blood and extrapolation to time zero, it is assumed that changes in patient samples are sufficiently negligible that no errors are introduced that will affect the results. It is possible, however, that such assumptions may not be warranted.

Recent investigations have shown that the undesirable products from labeling HSA with technetium may introduce errors when the procedure requires the dilution technique, as does the determination of plasma volume *(2)*. For example, depending on the reducing agent, as much as six to seven percent of the Tc-99m may be incorporated in a colloidal formation. The molecular weight of this colloid is greater than 300,000 and is extracted from the blood pool by the reticuloendothelial system (RES), particularly the liver. In addition a colloid somewhat smaller than HSA, has been defined in Tc-99m HSA preparations, and the quantity obtained varies with the kit manufacturer. As observed by scintillation scanning the in vivo distribution of this smaller colloid appears to be similar to that of HSA; however, animal autopsy data reveal significant differences in the blood pool compartment. The regeneration of $^{99m}TcO_4^-$ from the colloid is also similar to that observed from Tc-99m-labeled HSA. The lability of Tc from the pure colloid or pure HSA has been demonstrated in vitro and in vivo (within 20 minutes after injection) by the demonstration of Tc concentration in the stomach and urinary bladder. The lability of the bond may be a combination of both physical and metabolic factors.

After the intravenous administration of Tc-HSA, large colloidal particles are extracted by the RES, and regenerated $^{99m}TcO_4^-$ is concentrated in organs outside the blood pool. Both of these characteristics of Tc-labeled HSA will result in greater plasma dilution when compared to the

standard, and an overestimation of the plasma volume. Yet the technetium-labeled HSA results compare favorably with results from the "standard", iodinated-HSA. The extrapolated values from timed specimens should provide a relatively accurate estimate of the distribution of the labeled albumin. During the first ten minutes of equilibration after injection of the tracer, both the loss of radioactivity by phagocytosis of colloidal particles and the lability of the bond, however, could introduce errors that may be in excess of ten percent. Despite extensive investigations and evaluations and a feeling of confidence in the procedure, new evidence continues to surface, indicating errors in the determination of plasma volume by current techniques. Thus, if there is a problem it may not be with the technetium-labeled product but rather with the comparison standard.

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REFERENCES

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