18 fluoride, which subsequently moves from the ECF space to bone substance, using bromide ion as the ECF marker (*3*). The myocardial cell acts as a thallium sink, so that less of the ion is present at the venous end of the capillary than in an organ which does not concentrate thallous ion, because of the bidirectional flow. Thus A-V differences for thallous ion will be greater in the heart than in nonconcentrating organs, including the body as a whole, and if one evaluates extraction efficiency by A-V differences, instead of by intercompartmental rate constants, it will spuriously appear that a concentrating organ has a higher value than does the whole body, exactly what Melin and Becker found.

The authors have "corrected" their perfectly valid conclusion that the fraction of cardiac output delivered to the left ventricle by thallous ion is identical to that of microspheres by subtracting the amount of ^{201}Tl which appears in the lungs. Why pick on the lungs? From mathematic considerations, there is absolutely no valid reason to subtract the amount of thallous ion in the lungs. The lungs do not behave as a compartmental sink and are in free communication with the central vasculature, just as is every other organ which receives thallous distribution. In any mammillary/catenary compartmental arrangement, the presence or absence of a compartment not directly connected to the compartment under study has no influence or effect on instantaneous tracer movement into or out of the study compartment. In other words, what is going on in the lungs (simple passive diffusion of thallous ion into the ECF) has no effect on fractional cardiac output to the heart.

The tabular data published by the authors makes it quite clear that under each of the perturbations studied, the distribution of thallous ion is not significantly different from that of microspheres. They have shown that [^{201}Tl]chloride uptake is an excellent measure of global left ventricular flow.

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REPLY: Dr. Charkes is concerned about two methodological issues: the measurement of myocardial and total-body thallium extraction fractions, and the correction of injected thallium dose for lung uptake. We agree that the extraction of thallium (as well as any other permeable substances) is dependent upon factors other than blood flow, but we do not agree that "it is necessary to sample the ECF space" in order to measure extraction fraction. We used the double tracer method (*1*), a modification of the technique originally described by Chinard et al. (*2*) and Crone (*3,4*). The method assumes that there is no significant back diffusion and that the two tracers follow the same intravascular course (i.e., that the intravascular transit curves of the two substances are equal). Our data suggests that these assumptions were in fact met during our experiment. The instantaneous extraction fraction, calculated from each 3-sec venous blood sample, quickly reached a plateau value after appearance of the bolus and usually varied <5% over the next 15–20 sec. The constancy of these measurements is consistent with the absence of back diffusion. In addition, kinetic measurements have shown that back diffusion of thallium-201 is slow, in fact, much slower than other potassium analogs, such as potassium-43 (*5*).

Our data show that the fractional uptake of thallium by the myocardium overestimates the fractional distribution of cardiac output by ~15%. This appears to be explained by a higher extraction fraction of thallium by the heart compared to the total body, which, in turn is probably related to either reduced extraction through the high flow renal circulation, or inability of thallium to cross the blood-brain barrier, although rapid back diffusion from one or more noncardiac organs cannot be ruled out as an additional factor. Dr. Charkes comments that "if one evaluates extraction efficiency by A-V differences, instead of by intercompartmental rate constants, it will spuriously appear that a concentrating organ has a higher value than does the whole body." It is our understanding, however, that what is meant by the term "extraction fraction," is precisely the A-V difference present on the first pass through the organ. We should point out that our method measures only the net fractional passage of tracer across the capillary membrane without differentiation between intracellular and extracellular compartments. While Dr. Charkes' approach may be used for measuring total cardiac output, the fractional distribution of cardiac output cannot be determined by his method unless the rate constants for transfer of tracer from intravascular to extracellular fluid for each organ are known.

The correction for lung uptake is necessary because the lungs do, in fact, represent a "compartmental sink." After i.v. injection, ~5–10% of the thallium is extracted by the lungs in the first pass and fails to reach the left ventricle for distribution to the systemic organs. It is as though 5–10% of the planned injected dose remained in the syringe. Furthermore, the portion of the injected dose trapped in the lungs is not immediately mobilized for distribution to other organs since, similar to the heart, the net loss over time is slow. We estimated the fraction of the injected dose unavailable to the systemic organs by calculating lung content of thallium at 10 min after injection, the time that thallium content of the heart was compared to microspheres.

We agree with Dr. Charkes that "thallium-201 chloride uptake is an excellent measure of global left ventricular flow," and we believe that for precise and accurate quantitation of flow, attention must be paid to the differences in extraction existing between the heart and other organs.

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Correction Factor for Left Ventricular Volume Measurement

TO THE EDITOR: The articles by Melin et al. (*1*) and Verani et al. (*2*) published in the December 1985 issue of the Journal of Nuclear Medicine note a systematic deviation in radionuclide volume determinations.

My impression is that both papers start from a systematic error when assuming a relation between counts at the camera and counts originating at the target volume. To be more specific, in the simple experimental arrangement considered in the referred papers for phantom measurements, with a counting area defined at the camera by a two-dimensional region of interest (ROI) and a preferential direction along an axis perpendicular to the detector and going through the target volume (attenuation direction), we can assume a counting geometry based on very thin (dx) slices of the target volume. Those slices are of areas circumscribed by the ROI, located at positions starting at $x = 0$ up to $x = d$ along the attenuation axis. From $x = 0$ up to the detector interface the distance is L. If the counts originating at slice x are dS (x) and they are recorded at the camera as dC counts, then:

$$dC_{ROI} = K \cdot d\,S\,(x) \cdot \exp(-\mu\,(L - x).$$

Now it is important to note that both members of this relation are in different coordinate systems (the left one at the camera, the right one at the target volume). K is an efficiency counting factor that relates both counting coordinate systems. Then it is obvious that you can not move terms from one side to the other before integrating: this is the systematic error incurred by the referred authors.

To produce simple expressions, let us assume a rectangular or cylindrical geometry, for the target volume and detector, along the attenuation axis; then:

$$d\,S\,(x) = s\,A \exp(-\mu dx)\,dx$$

$$= s\,A\,dx.$$

where we assumed that attenuation through the slice is negligible, s is the radioactive (volumetric) concentration (homogenous) and A the cross-section of the target volume. Then

$$d\,C_{ROI} = K\,s\,A \exp(-\mu\,(L\text{-}x)\,dx.$$

Integrating for an interval of time across the ROI is the camera system and from $x = 0$ up to $x = d$ in the target system, we have

$$C_{ROI} = K\,s\,A\,\frac{1}{\mu} \exp(-\mu L)\,(\exp(\mu d) - 1).$$

Then, for the physical volume of the target (a number independent of both coordinate systems) we can write

$$V_t = Ad$$

$$= R\,C_{ROI}\,\frac{\exp(\mu L)}{\exp(\mu d) - 1},$$

where $R = \mu d/(sK)$. By doing measurements under similar geometrical conditions for a target sample (blood standard), using the same ROI at the camera, we can estimate μ (broad geometry), s and K:

$$C_{ROI}\,(\text{standard}) = K\,[s\,A\,\frac{1}{\mu} \exp$$

$$(-\mu L)\,(\exp(\mu d) - 1)]\ \text{standard}.$$

From this standard measurement, we can estimate R, required for the estimation of Vt.

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REPLY: Dr. Vergara correctly points out that the rigorous relation between ventricular volume and region counts differs from the simplified expression utilized by ourselves and others:

$$V = KC_{ROI}\,e^{\mu T},$$

where K = constant; C_{ROI} = counts in LV region of interest; μ = attenuation coefficient; T = distance of the volume centroid from camera. As previously pointed out by Links et al. (1), the rigorous expression obtained by integrating the extended source volume is:

$$V' = KC_{ROI}\,e^{\mu T}\,\frac{\mu d}{e^{\mu d/2} - e^{\mu d/2}},$$

where, T = distance of volume centroid from camera and d = mean thickness of radioactive volume. By replacing $L = T + d/2$ in expression 5 mentioned by Vergara, this same expression is obtained.

The correction factor imposed by extended source geometry is then:

$$\frac{V'}{V} = \frac{\mu d}{e^{\mu d/2} - e^{-\mu d/2}}.$$