patient study may not be well established as is the case for a phantom, but, nevertheless, the variability between algorithms can be determined. The major difficulty of using such a software phantom or library is the incompatibility between the patient file structures of different computer systems, which, at this time, tends to restrict any survey to systems of similar design. It would be desirable if programs that allow interchange of patient studies between different systems could be made more generally available in order to facilitate these types of comparisons.

The conclusion that could be drawn from the results of Makler et al. is that EFs do not vary significantly from one system to another—at least in the hospitals included in their survey. We would caution against extrapolation of such a conclusion on a wider basis. We have shown how the EF for the Vanderbilt phantom might vary by virtue of the algorithm used for background subtraction (*5*). Other factors may also play an important role. Consequently, it is very necessary that the range for normals be determined in each individual institution and, if different algorithms are used on different systems within the same institution, it will be necessary to establish the normal range for each.

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REPLY: We thank Drs. Cradduck and Busemann-Sokole for their thoughtful comments regarding our manuscript. They have shown (and we agree) that the Vanderbilt cardiac phantom does not exactly simulate cardiac physiology. However, we do not feel that their observations invalidate the conclusions of our study.

Our study used the phantom to provide identical input data to the 11 institutions surveyed in order to assess the variability in ejection fraction (EF) calculations. If we had found excessive variability, the issues raised by Drs. Cradduck and Busemann-Sokole could have been the cause; however, we observed low variability between institutions, suggesting that the calculated values were precise. Whether the problems with background assessment would affect the *accuracy* of the determined values was not addressed in our study since it concerned itself only with reproducibility.

Doctors Cradduck and Busemann-Sokole raise an important point regarding the fact that the three attenuators are labeled, and thus the results could have been biased. Our three attenuators are labeled 25%, 35%, and 75%, but the calculated EFs averaged 37%, 52%, and 82%, respectively. Thus the operators probably thought they were reporting incorrect values. The agreement between institutions under these conditions confirms the precision of the calculated results. The differences between the labeled EF and the observed EF may well be related to the errors in background determination, but are irrelevant to an assessment of reproducibility. Of interest, the difference between the MDS and DEC computers noted in the low EF range could possibly be caused by differences in the background algorithms, but we do not have information regarding this point.

In summary, while we agree that the Vanderbilt cardiac phantom may not be the most suitable "gold standard" for cardiac function, we do feel that it was appropriate for a reproducibility survey of this nature.

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Schilling Evaluation of Pernicious Anemia

TO THE EDITOR: We read with interest the paper "Schilling Evaluation of Pernicious Anemia: Current Status" (*1*) and agree that the exchange of B_{12} moieties can occur on the intrinsic factor molecule leading to difficulty resolving clinical diagnoses with the dual isotope Shilling test (DIST). However, statistical uncertainty could account for much of the scatter in their Fig. 1, which shows the distribution of DIST results by Bound/Free (B/F) ratio and free Cobalt-58 (^{58}Co) B_{12} excretion.

In situations involving measurement of count rates, the smaller the difference between sample and background rates, the greater the total count required to reduce the error to a given level. Evaluation of the background corrected free ^{58}Co B_{12} excretion and B/F ratio from the DIST involves two and six subtractions, respectively. To demonstrate the effect of total count variation on the uncertainty in the free ^{58}Co excretion, consider the expression (*2*):

$$\text{Free } ^{58}\text{Co excretion} = (X)(Y),$$

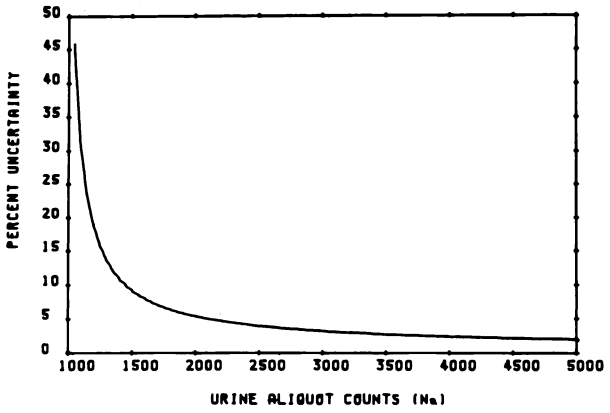

FIGURE 1
For given amount of standard and background activity (Ns = 25,000 and Nb = 1,000, respectively) percent uncertainty in error function Z_Y increases markedly as activity in urine aliquot (Na) approaches background activity

where X = (2%)(total urine volume)/(aliquot volume)

$$Y = \frac{\text{Total aliquot } {}^{58}\text{Co count} - {}^{58}\text{Co background}}{{}^{58}\text{Co standard} - {}^{58}\text{Co background}}$$

Using standard formulas for propagation of error (*3*) the uncertainty of Y can be estimated. The random error introduced by X does not depend on counting statistics and can be neglected.

$$Z_Y^2 = \frac{(Na - Nb)^2}{(Ns - Nb)^2} * \left(\frac{Na + Nb}{(Na - Nb)^2} + \frac{Ns + Nb}{(Ns - Nb)^2}\right),$$

where Na = Urine aliquot counts; Nb = Background counts; and Ns = Standard counts. The percent uncertainty in Y is given by $Z_Y/Y^* 100\%$.

Plotting the percent uncertainty in Y against Na for a given Nb and Ns (figure) shows that as the difference between Na and Nb decreases, the uncertainty in Y, and consequently in the percent free ^{58}Co excretion, increases markedly. The error in the B/F ratio likewise increases as Ns − Nb decreases, but even more rapidly than for the free ^{58}Co excretion alone. This combination of errors is necessarily greater than the error in either individual percent excretion.

Before conclusions can be drawn regarding sources of error with the DIST, such as isotopic substitution, it is essential to clearly document that adequate total counts have been obtained, particularly from the urine aliquots.

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REPLY: In our recent article on the Schilling test we reviewed the phenomenon of crossover of vitamin B_{12} moieties contributing to the incidence of nondiagnostic test results. Graham and Smith have aptly stressed the significance of statistical variation in the performance of Schilling examinations.

While the crossover of B_{12} moieties cannot be prevented simply in the routine administration of the dual-isotope Schilling examination, the contribution of statistical errors may be reduced by use of a sensitive well-counter and extended counting periods. With use of a 3″ NaI(Tl) crystal and 20-min counting interval, our counting data demonstrated an average cobalt-58 (^{58}Co) background of 770 counts and ^{58}Co standard of 121,000 counts. As demonstrated in Fig. 1, with these values the contribution of counting errors in B_{12} excretion is significantly reduced compared to the example of Graham and Smith. It should be noted that the counting efficiency of the energetic 810 kev ^{58}Co gamma rays is greatly diminished with use of thinner counting crystals.

We concur with Graham and Smith regarding the importance of counting factors in addition to the refractory problem of vitamin B_{12} crossover. By paying careful attention to the technical aspects of this test, its maximum benefits may thus be realized.

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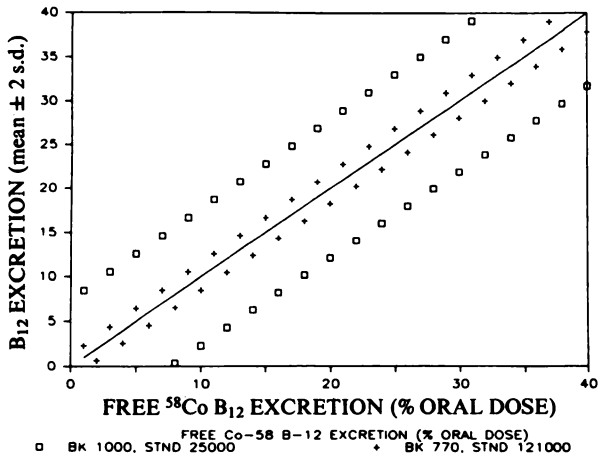

FIGURE 1
Predicted values (mean ± 2 standard variations) of measured ^{58}Co vitamin B_{12} excretion compared with actual B_{12} excretion. Graham and Smith's theoretical values (□) are shown in comparison with our actual average values (+) based on 1 l 24-hr urine collection. Our smaller statistical variation reflects improved counting statistics