First, in figure 4, the authors present the weighted tolerance limits about the regression lines according to Miller. However, this technique is not mentioned in the reference given by the authors. Only unweighted tolerance limits are discussed. We would appreciate if the authors could give us a more pertinent reference on this topic.

Second, in the Methods section, the authors state that variation about the regression line is a function of the body surface area, thus justifying the use of the weighted regression model. However, they do not describe how this function was estimated. The reference given does not discuss this. Again, we would be glad if the authors could provide us with some references on this subject.

Finally, in order to determine the existence of such functions relating body surface area to variation about the regression line, we found the coordinates of the points appearing on three graphs of figure 4 (RVAWD, RVDD and PAD), by making photographic enlargements. The residuals were then analyzed for the three variables according to the techniques of Draper and Smith. It was found that the variation about the regression line was not a function of the body surface area. Unweighted regression seemed inadequate. Moreover, the unweighted regression technique gave the same regression lines as those found by the authors, but the goodness of fit was far less. Table 1 shows the value of the multiple squared correlation coefficients found by using the unweighted regression technique compared to those calculated by the weighted regression technique of the authors.

In conclusion, unless adequate answers can be given to the problems we have discussed, we are forced to consider that the regressions shown are questionable and that the validity of the conclusions drawn can be seriously doubted.

The authors reply:
To The Editor:
We thank Drs. Ducharme, Lepage and Davignon for the interest they showed in our paper. Miller describes a technique for using the Bonferroni inequality to combine a confidence interval for a regression line with a confidence interval estimate of the error variance to produce a tolerance interval. The application of this technique to weighted multiple regression was discussed in the appendix of our original manuscript. Space restriction did not permit publishing of this appendix. We will supply it upon request.

With regard to choice of a weighted regression model vs an unweighted model, our examination of residuals showed a tendency for increasing variance with increasing body surface area. This is similar to other variables in children with respect to growth, such as height, weight, and skull circumference. This was particularly marked for aortic root, left atrial, and left ventricular diastolic dimensions. The increasing variance was less marked for right ventricular anterior wall in diastole, right ventricular diastolic dimension or pulmonary root dimension. We decided to simplify the presentation by using the same analysis for all dependent variables. The weighted analysis appeared to be the superior choice because the objective of the statistical analysis was to provide estimates of the normal range.

Three points must be considered:
1) The tolerance interval method of Miller is conservative; that is, the estimated tolerance limits may be larger than is strictly necessary;
2) The effect of a model that implies increasing error variance with increasing body surface area is to provide a relatively smaller tolerance interval for smaller body surface area;
3) The tolerance intervals provided by unweighted regression were so wide for lower values of body surface areas that a useful guide to normal ranges was not provided.

We are puzzled by the inference that the fact that weighted and unweighted regression produced similar coefficient estimates but small $R^2$ implies that weighted regression is invalid. Both weighted and unweighted regression produce unbiased estimates of the regression function. If the weighted model is appropriate, it will produce a smaller estimate of error variance and consequently large $R^2$.

In our paper we showed in figure 5 that at the extremes of measurement, newborn and adult data had a range similar to those obtained in our paper. In addition, it now appears that the data from Epstein et al. noted in our paper, have been revised and are presented in a different form. These data appear in close agreement with our data in terms of confidence intervals.

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References

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To the Editor:
The recent study by Miura et al. measured infarct size by a macroscopic pathologic technique which, as the authors themselves suggest, is open to criticism. In our laboratory, a very similar

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