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Response From Authors

Dr. Taylor (referencing Dedrick and Davis [1]) states that the correlation coefficient r is a measure of association between variables but does not necessarily imply agreement. He suggests that our highly significant P value (which we obtained when we compared FP and VAC results for GHb [2]) does not necessarily indicate good clinical agreement. Furthermore, he states that linear regression is not the best approach for comparing two methods where both are imprecise, and suggests that a plot of the difference against the mean for each pair of results would allow a straightforward clinical interpretation. Such a plot is appropriate to examine agreement between the two measures but not the association that was our intent.

Our purpose was to examine the relative position of a subject on the two measures as quantified by the correlation coefficient. That is, we wished to investigate whether a subject with a high reading on FP would have a high reading on VAC, and whether one might expect intervention leading to a decrease in VAC would be reflected, similarly, in a decreased FP reading. Figure 1 in our paper presented the pictorial view of this association, which can be used to predict one value from the other via the regression equation (2). The laboratories' established means and ranges of normal controls are not the same for the two tests (FP: range 5.82–7.58%, mean 6.70%; VAC: range 6.3–8.2%, mean 7.25%). This tells us that values are not interchangeable and do not meet Taylor's definition of "agreement" a priori. Thus, the regression equation was included to allow interested readers to evaluate the correspondence themselves, and our suggestion that one measure should be used consistently was intended to highlight the lack of equivalence in results.

Our classification of scores as multiples of the method SD results in 59% comparably classified, with a kappa statistic of 0.44 (3) indicating fair to good classification agreement. Dr. Taylor suggests excluding the most extreme group of 16 subjects with results >10 SD above the mean. These 16 subjects are 27.6% or our sample. Given that the mean for FP results was 9.3 SD above the mean of controls and the average VAC reading was 8.1 SD above the mean of controls, eliminating these extremes would not appear to be justified in evaluating the test for use with diabetic subjects. Furthermore, in an earlier publication (4), we reported that among 588 diabetic subjects in the Colorado IDDM Registry average HbA_1 levels as measured by the FP method were 10 SD above the mean for normals.

We recognize that methods for comparing clinical measurement technique are the subject of considerable discussion. We appreciate Dr. Taylor's attention to this methodology and his recent work assessing GHb methods (5). We agree that differences between methods should be evaluated carefully. However, it was not our intent to say that results from the two methods are interchangeable. Rather we wished to demonstrate that the filter paper method is a useful tool for epidemiological research because it accurately classifies the level of glycemia. We apologize for confusion we may have perpetrated in this regard. The Spearman rank correlation is designed to evaluate relative rank in two samples, not agreement between the two measures; and the SD cross classification results add weight to our assertion that subjects will fall in similar relative positions on the two measures.

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FP, FILTER PAPER AFFINITY CHROMATOGRAPHY; VAC, VACUTAINER ION-EXCHANGE CHROMATOGRAPHY.

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Response From Authors

In response to questions about day 7 elution for the filter paper assay, Dr. Taylor is absolutely right that we have not published any data validating this modification from day 14 elution. The decision to further evaluate the day 7 elution procedure after we published the original method was made for practical reasons; the shorter time period would allow us to return results faster. We now have data relating day 7 filter paper elution results to GHb measured by affinity chromatography from frozen hemolysates. As with the day 14 elution, the correlation is excellent ($n = 412$, $r = 0.96$, $P < 0.0001$).

In response to Dr. Taylor's comment about the affinity chromatography method being susceptible to changes in experimental protocol, most GHb methods are susceptible to changes in experimental protocol. We have decreased the variability of our affinity chromatography assay by standardization to a reference method. We include calibrators in each assay that have values assigned by a designated reference method (1). In doing so, we are able to decrease the assay variability; CVs for our standardized affinity assay have been <5% for the past several years.

We are in complete agreement with Dr. Taylor that differences between methods should be assessed carefully. In view of the fact that, at the present time, there is no consensus on either a standard or reference method for GHb, absolute results are not comparable between methods. We disagree with John et al. (Dr. Taylor's reference 9), however, that calibration material cannot be used to interconvert results for HbA_1, HbA_{1c}, and GHb. We have shown that our approach to interlaboratory standardization of GHb does allow direct comparison of results obtained by different methods, including those measuring HbA1, HbA1c, and total GHb (1).

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CV, COEFFICIENT OF VARIATION.

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