To the Editor:

Vieira et al. (1) used the Wallac Delfia immunofluorometric assay to demonstrate that macroprolactin is a common cause of apparent hyperprolactinemia, and this confirms our experience (2) and that of others (3). However, their data validating the polyethylene glycol (PEG) precipitation as a screening method for detecting macroprolactinemia are substantially different than ours (2) and appear to be inconsistent. They suggest that a recovery of >65% of serum prolactin (PRL) after PEG precipitation indicates the absence of macroprolactin; however, their Fig. 1 shows that samples giving such recoveries contained 10–40% high-molecular weight PRL as determined by gel filtration chromatography. Furthermore, the data shown in Fig. 1 of the recovery of PRL after PEG precipitation and the proportion of PRL present as the high-molecular weight forms determined by gel filtration show considerable scatter such that a sample showing 50% recovery after precipitation with PEG might contain 15–95% macroprolactin. Their reproducibility studies also showed considerable imprecision (CV, 7–28%) for the PEG precipitation technique, and this may be one contributing factor.

In my experience, the PEG precipitation test has been more reproducible (CVs, 5.8% and 6.5%) and more definitive. An initial report (2) demonstrated that in 69 cases with PRL >19.4 µg/L (700 milliunits/L), the recovery of >40% of the PRL after precipitation with PEG identified all 52 samples containing only monomeric PRL but included one sample containing 10% of the immunoreactive PRL as macroprolactin. A recovery of <40% identified all 16 samples containing substantial quantities of macroprolactin (34–90% of the immunoreactive PRL).

I have now used precipitation with PEG to examine 195 samples with total PRL >19.4 µg/L (700 milliunits/L) over a 38-month period. Using a conservative cutoff of 50%, I found low recovery after PEG precipitation in 30 samples (15.4%); the presence of macroprolactin was confirmed by gel filtration chromatography in all but one sample. Similar results were obtained in a neighboring district, with macroprolactin identified in 25 of 145 (17.2%) samples. These data are summarized in Fig. 1 and demonstrate that when macroprolactin is present it is the predominant immunoreactive form of PRL present. When no macroprolactin is present, gel filtration chromatography shows no peak of higher molecular weight PRL.

The reasons for the differences between my experience with PEG precipitation and that of Vieira et al. (1) are not immediately apparent. I have used a similar technique with identical reagent concentrations but use reagents at room temperature, whereas Vieira keep their PEG at 4 °C. Temperature affects the recovery of PRL after precipitation with PEG (2), and this may be a source of variation. However, most of the differences may be related to their definition of the presence or absence of macroprolactin on gel filtration chromatography. It is not clear whether a clearly defined peak of macroprolactin was demonstrated in all samples categorized as containing high-molecular weight forms of PRL, and it would be most helpful if representative chromatograms were published so that the efficiency of the separation can be seen.

In my experience, macroprolactin is a common cause of apparent hyperprolactinemia and a cause of diagnostic confusion, which may lead to inappropriate treatment. I agree with Vieira et al. (1) and Lindstedt (4) that all samples showing apparent hyperprolactinemia should be examined for macroprolactin; however, it should be noted that although all commercial assays for PRL investigated thus far react with macroprolactin (albeit to a varying extent), not all of these assays can be used with the PEG precipitation technique (2). Centrifugal ultrafiltration may provide an alternative means of demonstrating the presence of macroprolactin (5), and additional work is in progress to validate this technique.

References

1. Vieira JGH, Tachibana TT, Obara LH, Maciel RMB. Extensive experience and validation of

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Two of the authors of the Technical Brief cited above respond:

To the Editor:

M. Fahie-Wilson makes several interesting points to which we would like to respond. First, we agree that a recovery of >65% does not indicate the absence of macroprolactin, but that macroprolactin is not the predominant form in circulation. Regarding the imprecision of the polyethylene glycol (PEG) precipitation technique, it is worth considering that the highest values were observed in the sample with a recovery in the intermediate range (47%) and in the sample with very low recovery (5%) (1). The slight differences in the PEG precipitation processes, especially those relating to temperature and centrifugation, can help to explain the differences observed when comparing our results with those of Fahie-Wilson and Soule (2). Another important point is the definition of “substantial quantities of macroprolactin”; we arbitrarily defined that >50% of the circulating prolactin in the form of macroprolactin should be considered as a substantial quantity; however, this definition obviously depends on the total prolactin present in the sample. Samples with high prolactin values and substantial quantities of macroprolactin could still have monomeric prolactin in sufficient quantities to induce clinical symptoms. As a last point, we would like to stress that the chromatographic system adopted by Fahie-Wilson and Soule (2) has a better resolution than the one that we used. Our choice of a simpler and more rapid system stems from practical necessity.

Finally, we would like to add that the Fahie-Wilson and Soule publication (2) was not available during the preparation of our Technical Brief, which was very unfortunate, because access to their data would have allowed us to produce a more comprehensive publication. Nonetheless, calling attention to the macroprolactin phenomenon and providing a practical way of dealing with it are the objectives that, in our understanding, were fulfilled by the publications.

References

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Point-of-Care Testing Outcomes in an Emergency Department

To the Editor:

In response to your Editorial (1) on outcomes assessment for point-of-care testing (POCT), we would like to convey our comments on our own experience with POCT in our hospital emergency department (ED). We introduced a NOVA 14 whole blood electrolyte analyzer (on loan from VA Howe and Co., Ltd) into our ED for a trial period. Result turnaround times (from blood sampling to result availability) and total patient waiting times in the ED were measured in three settings: (a) use of POCT in the ED; (b) use of a pneumatic tube transport system to carry samples to the central laboratory, with results returned electronically; and (c) use of a pneumatic tube rapid transport system instead of a porter system. The procedures followed were approved by our ethics committee. The turnaround time for results using POCT (median, 5 min; 25th to 75th centile range, 4–6 min; n = 130) compared with a porter system (median, 58 min; range, 47–77 min; n = 191) or a pneumatic tube rapid transport system (median, 49 min; range, 37–65 min; n = 192) was significantly faster (P <0.05, Wilcoxon sign-rank test), as expected.

The shorter turnaround time for laboratory test results did not reduce total patient waiting time (median, 219 min; range, 171–277 min with POCT; median, 212 min; range, 170–275 min with the porter system; and median, 258 min; range, 189–364 min with the rapid transport system).

Other factors, such as reduced bed availability on the wards at the time the pneumatic tube transport was used and delays associated with other investigations (such as radiology, enzymes, drug assays, and blood cell counts, with a median turnaround time of 80 min) had a greater impact on patient disposition.

Preanalysis delays were related to the organization of doctors’ time in the ED (median, 120 min). A critical path analysis illustrating the median times for 1 night of the study is shown in Fig. 1.

It was our impression that with training, the ED staff could routinely obtain analytically acceptable results with POCT but that the laboratory