were linear between 10% and 100% for SimulTrac and Quantaphase II.

Linearity of the assays was tested in duplicate, and statistical methods produced a flat response. Comparison methods, the AxSYM (Quantaphase II) method, appeared to be present when folate was measured in erythrocyte hemolysates. At concentrations >906 nmol/L (>400 μg/L) with the SimulTrac method and >453 nmol/L (>200 μg/L) with the Quantaphase II method, the regression lines were found to bend. We saw no erythrocyte folate results >1360 nmol/L (>600 μg/L) by the AxSYM method, even in patients known to be taking folate supplements regularly for a protracted period of time.

We conclude that the dynamic range of the AxSYM folate assay does not extend above 23 nmol/L (10 μg/L) for serum folate and not above 1360 nmol/L (600 μg/L) for erythrocyte folate. This is only half the dynamic range of other protein-binding folate assays.

References

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Editor’s Note: A representative of the manufacturer declined the opportunity to reply.

Limited Linear Range of the Abbott AxSYM Serum and Erythrocyte Folate Methods

To the Editor:
Recent studies have clearly demonstrated that plasma homocysteine is an independent risk factor for atherosclerosis (1, 2). Although increased serum homocysteine is genetically determined, increasing dietary folate (3) can significantly lower the values. Indeed, the US Food and Drug Administration has recently increased the daily dietary guidelines for folate intake, and since January 1998 wheat flour-based foods have been supplemented with folate (4, 5). Decreased folate during pregnancy is also a strong risk factor for neurological birth defects (6). Historically, plasma and red blood cell (RBC) folate determinations have been performed to assess folate deficiencies in investigations of macrocytic anemias, and little or no clinical information was ascribed to normal or increased folate values. However, the recent goals of reducing serum homocysteine and maintaining high folate concentrations during pregnancy suggest that examination of serum and RBC folate concentrations with an interest in higher values may become common. Indeed, it has been recommended by some that the lower limit of the reference range for plasma folate be raised by 250% (7). Thus, it is likely that folate concentrations will be increased in the population and that accurate determination of high as well
as low folate concentrations will be important.

Historically, there are wide variations in folate analytical results (8). At our institution, plasma and RBC folate concentrations are determined using the Abbott AxSYM microparticle enzyme immunoassay method. We previously had determined that the upper range of linearity for this method was 14 \( \mu \text{g/L} \) by diluting samples with folate concentrations >25 \( \mu \text{g/L} \). We have thereafter used a 1:2 sample dilution buffer (unpublished data). The manufacturer claims the method to be linear to 20 \( \mu \text{g/L} \), whereas it was 168\% for samples with folate values >15 \( \mu \text{g/L} \). Essentially identical findings were observed for RBC folate samples having a value >10 \( \mu \text{g/L} \) on the AxSYM Folate radioassay. We measured the AxSYM values from undiluted samples with values >10 \( \mu \text{g/L} \). On the basis of these findings, we now dilute all plasma and RBC samples 1:2 using Abbott sample dilution buffer when the folate concentration is >8 \( \mu \text{g/L} \). Currently, this represents 71\% of our samples, making use of the Abbott AxSYM somewhat cumbersome to the laboratory.

Fig. 1. Plasma folate values from 526 samples averaged from undiluted and diluted 1:2 (x-axis) vs the undiluted plasma folate AxSYM values minus the 1:2 diluted values for the same 526 samples (y-axis; mean = -3.68 \( \mu \text{g/L} \)).

Values were obtained from two separate AxSYM analyzers and four separate calibrations.

### References


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Editor’s Note: A representative of the manufacturer declined the opportunity to reply.