

Patient sample management, (standardization, harmonization, reference ranges, etc)

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REFERENCE INTERVAL FOR SERUM FOLATE MEASURED WITH AN ASSAY TRACEABLE TO THE WHO INTERNATIONAL STANDARD

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BACKGROUND: Most folate immunoassays have been recently recalibrated to the WHO International Standard-NIBSC 03/178 to improve inter-assay harmonization. However, we observed that the recalibration of Roche Diagnostics Folate III assay yielded a significant shift in the average folate measured values, with a #50% difference vs. the old Roche assay at concentrations around the lower reference limit (LRL). Here we report data from apparently healthy individuals obtained with the WHO-recalibrated assay for defining the traceable reference interval for serum folate.

METHODS: We enrolled 322 healthy blood donors (50% males; median age, 45.5 years) with haemoglobin and erythrocyte MCV values within reference limits and not undertaking folic acid supplementation. Serum samples were measured by using WHO-recalibrated Roche Folate III assay (code 07559992190) on a Cobas 6000 analyzer ($CV \leq 7.2\%$ and limit of detection of $0.6 \mu\text{g/L}$). Reference interval derivation was according to CLSI C28-A3c standard. Multiple regression models were used to estimate the influence of age, gender, Italian origin, smoking habit and portions of consumed fruit/vegetables on folate concentrations.

RESULTS: We found no gender-related difference. Folate median (25-75th percentile) concentrations were $4.1 (2.9-5.6) \mu\text{g/L}$. The estimated reference interval [2.5-97.5th percentile limits (90%CI)] was $1.3 (1.1-1.4) - 9.8 (8.6-12.2) \mu\text{g/L}$. Notably, the LRL was markedly lower than the one ($3.3 \mu\text{g/L}$) previously estimated by us using the old Roche assay on a similar population. Folate values significantly ($P < 0.001$) increased with age and with the number of taken portions of fruit/vegetables per day (adjusted R^2 , 18.9%), with no influence by smoking and non-Italian origin.

CONCLUSIONS: Our experimental estimate of LRL using Roche WHO traceable assay on a population free of folate supplementation reveals that this value is far lower than that reported by the manufacturer in the assay package insert ($3.9 \mu\text{g/L}$), likely including fortified subjects. Laboratories using folate assays harmonized to NIBSC 03/178 material may adopt the LRL of $1.3 \mu\text{g/L}$ to detect vitamin deficiency, providing that there are no differences in test results across populations due to biological or environmental factors.