

Letter to the Editor

External quality control of urinary methyl malonic acid quantification – announcement of a pilot study

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Methylmalonic acid (MMA) accumulates in the body in cases of cobalamin (vitamin B₁₂) deficiency because of impaired metabolization of methylmalonyl CoA to succinyl CoA by methylmalonyl CoA-mutase, a cobalamin-dependent enzyme. Therefore, MMA represents a functional marker of cobalamin deficiency (1). It is widely accepted that MMA measurement is useful and necessary if serum cobalamin concentrations between 150 and 300 pg/mL are found, overcoming the limited reliability of serum cobalamin measurement in the lower concentration range (2–4). Despite good evidence for the usefulness of MMA measurement, tests are rarely requested in many countries and are offered by only a few laboratories. This particularly applies for measurement of urinary MMA, which clearly represents the sample material of choice; impaired renal function is associated with increased serum and plasma MMA concentrations, irrespective of the cobalamin status (5). In contrast, measurement of urinary MMA concentrations and calculation of the ratio of urinary MMA to urinary creatinine is essentially independent of individual renal function.

Quantification of MMA in both serum and urine is technically demanding and gas chromatography (GC) or liquid chromatography (LC) isotope dilution mass spectrometry methods are mandatory. So far, no matrix-based materials for MMA assay calibration and continuous quality control are commercially available. After initial studies (6, 7), proficiency testing programs for serum and plasma MMA measurement were implemented in Europe and the USA. For urinary MMA measurement, however, no external quality control programs have been implemented so far.

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With this letter we would like to announce an international pilot project for the implementation of a proficiency testing program for urinary MMA measurement. The main objective of this study is to assess the reliability of analytical methods used for MMA measurement and to investigate the degree of inter-laboratory variability of urinary MMA measurement. Such data are important for the interpretation of MMA results by clinicians.

For the purpose of this study, pooled urine samples of four MMA concentration levels have been prepared in a professional setting (Chromsystems GmbH, Munich, Germany). Samples are lyophilized and can be shipped by regular postal services. Readers of *Clinical Chemistry and Laboratory Medicine* are invited to join this pilot study. If they decide to do so, they are asked to send an e-mail to Michael Vogeser, University of Munich (michael.vogeser@med.uni-muenchen.de) up until March 31, 2005 with the detailed postal address of the participating laboratory; samples will be shipped within 1 week. Analysis results can be submitted via e-mail. Six weeks after the end of the shipment period the results will be processed and the data (with mean concentrations reported and distribution of results) will be sent to the participants. The identity of the participants will not be given to any third party.

It is planned to submit the results of this pilot study as an article to *Clinical Chemistry and Laboratory Medicine*. Demonstration of close inter-laboratory agreement of urinary MMA measurement by an international survey is, in our opinion, essential to increase the limited acceptance of urinary MMA measurement by clinicians, and thus has the potential to improve patient care.

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