URINARY METHYLMALONIC ACID AND COBALAMIN DEFICIENCY IN THE ELDERLY

To the Editor:

The study by Drs. Norman and Morrison made very interesting and informative reading. The high prevalence and availability of therapy for cobalamin deficiency in the elderly make any noninvasive diagnostic index valuable. In this context, I would like to draw your attention to some additional data on this subject.

Yamauchi and coworkers studied the relation of urinary methylmalonic acid (MMA) excretion and Vitamin B₁₂ deficiency. They found that patents with neurologic disturbances excreted larger amounts of MMA than those without neurologic disorders. They also concluded that MMA could be a useful adjunct to distinguish megaloblastic anaemia from myelodysplasia with megaloblastosis.

As 2% of the general population are carriers of inherited methylmalonic acidemia, Rasmussen and Nathan examined the urinary excretion of MMA in patients with methylmalonic acidemia. They found urinary MMA levels to range from 1.18 to 2.48 mmol per mol of creatinine (reference range 0.58 to 3.56). This reveals that heterozygotes for inherited methylmalonic acidemia would not give false-positive results for cobalamin deficiency, and hence testing for urinary MMA remains useful in this subgroup.

Finally, Rasmussen has described the use of another method for the measurement of urinary MMA, anion exchange extraction using formate and formic acid. This technique was found to be both reliable and convenient for the evaluation of cobalamin deficiency, particularly in patients with normal or moderately reduced serum cobalamin levels.

The above data, in conjunction with the authors' study, promise to attenuate an important treatable cause of permanent neurologic disability in the elderly.

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MORE ON HDL SUBFRACTIONS

To the Editor:

I have read with interest the review on the HDL subfractions by Silverman et al. Essentially, the article deals with the two fundamental subclasses of HDL: HDL₂ (density 1.063 to 1.125 g/mL) and HDL₃ (density 1.125 to 1.210 g/mL). Two other subclasses are frequently referred to in the review: Lp(A-I with A-II) and Lp(A-I without A-II), based on the presence or absence of apoA-II in the HDL particle; both types occur within the IDL₂ and HDL₃ density ranges. The authors also mention a number of isolation methodologies other than ultracentrifugation and their disadvantages. One major disadvantage is the alteration of the lipoprotein particle, so that the related classification of HDL may not reflect the physiologic one. Quite appropriately, they state that "Measuring subfractions...may provide information not only about atheroerotic risk but also about the underlying physiologic mechanisms responsible for that risk." A novel technique (isotachophoresis) resolves HDL in at least six subpopulations, which differ for lipid and apolipoprotein composition as well as for their affinity of binding to the cell-surface HDL receptors. Indeed, the same apolipoprotein contained in different HDL particles assumes different conformations which profoundly affect its function(s). This consideration leads us to one aspect—function—dealt with in the first part of the review.

The range of functions exerted by apolipoproteins is wider than appearing from Table 1. Among these functions, of clinical relevance can be considered the process of repair and nerve regeneration, and the stimulated release of placental lactogen hormone. Another property of HDL apolipoproteins is interaction with thyroid hormones (T₄, T₃) via specific and medium affinity sites (one per molecule). At least for apoA-I and apoE, the two apoproteins studied in greater detail, the respective thyroid hormone binding domain is located in the exon-3 coded region, as opposed to the exon-4 coded lipid binding domain. As a result of this interaction, circulating HDL are the major apolipoprotein carrier for thyroid hormones. For instance, they carry 2% to 4% of total plasma T₄ versus about 0.2% carried by low-density lipoproteins (LDL) and 0.03% by very low-density lipoproteins (VLDL). The LDL-T₄ complex is internalized by LDL-receptor competent human fibroblasts, indicating that LDL delivers to