Cobalamin Status (Holo-Transcobalamin, Methylmalonic Acid) and Folate as Determinants of Homocysteine Concentration, Rima Obeid, Muhidien Jouma, Wolfgang Herrmann* (1 Department of Clinical Chemistry, University Hospital of Saarland, 66421 Homburg, Germany; 2 Department of Biochemistry/College of Pharmacy, Damascus University, Syria; * address correspondence to this author at: Department of Clinical Chemistry/Central Laboratory, University Hospital of Saarland, Bldg. 40, Kirberger Strasse, D-66421 Homburg/Saar, Germany; fax 49-6841-1623109, e-mail kchwher@uniklinik-saarland.de)

Concern has emerged in America about subtle cobalamin (Cbl; vitamin B12) deficiency, especially in at-risk population groups such as the elderly and vegetarians. A n

**Table 1. Metabolites and the B vitamins according to MMA quartiles.**

<table>
<thead>
<tr>
<th>MMA, nmol/L</th>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, n</td>
<td>83</td>
<td>84</td>
<td>83</td>
<td>83</td>
</tr>
<tr>
<td>Patients/controls, n</td>
<td>58/25</td>
<td>54/30</td>
<td>57/26</td>
<td>57/26</td>
</tr>
<tr>
<td>Age, years</td>
<td>54 (36–65)</td>
<td>50 (34–63)*</td>
<td>50 (36–64)*</td>
<td>50 (36–64)*</td>
</tr>
<tr>
<td>MMA, nmol/L</td>
<td>139 (95–168)</td>
<td>213 (176–265)*</td>
<td>326 (269–419)*</td>
<td>691 (456–2039)*</td>
</tr>
<tr>
<td>HCY, μmol/L</td>
<td>10.8 (6.3–18.0)</td>
<td>12.1 (6.7–19.2)*</td>
<td>13.0 (8.8–21.8)*</td>
<td>15.4 (9.3–31.0)*</td>
</tr>
<tr>
<td>holoTC, pmol/L</td>
<td>63 (19–300)</td>
<td>41 (21–157)*</td>
<td>34 (11–94)*</td>
<td>24 (2–48)*</td>
</tr>
<tr>
<td>Vitamin B12, pmol/L</td>
<td>274 (187–609)</td>
<td>240 (164–461)*</td>
<td>204 (134–372)*</td>
<td>189 (132–294)*</td>
</tr>
<tr>
<td>Folate, nmol/L</td>
<td>21.3 (10.9–34.0)</td>
<td>19.4 (10.9–38.7)</td>
<td>19.5 (11.6–32.1)</td>
<td>18.6 (9.7–37.2)</td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>71.6 (49.5–92.7)</td>
<td>72.5 (50.6–97.7)</td>
<td>74.3 (44.9–97.0)</td>
<td>75.1 (43.1–102.0)*</td>
</tr>
</tbody>
</table>

* Data are medians (5th–95th percentiles).

| b P < 0.05 compared with the first MMA quartile (two-tailed Mann–Whitney test).
chemical indices between cardiovascular disease (CVD) patients and controls (data not shown). Similarly, a previous report failed to confirm a frank link between Cbl deficiency and increased CVD risk (2).

The holoTC and serum Cbl concentrations were highest in individuals within the lowest MMA quartile (Table 1). In such a case, normal Cbl together with normal folate status may prevent HCY accumulation (median HCY, 10.8 μmol/L). However, in the highest MMA quartile, increased HCY (median, 15.4 μmol/L) may indicate impaired folate utilization despite normal serum folate. A role of Cbl in regulating folate metabolism has been suggested (12). Interestingly, given that HCY is an established CVD risk factor in the Syrian population (13), the median HCY concentrations in the first two MMA quartiles seem in accordance with the widely accepted cutoff value (18 μmol/L) above which HCY may become a risk factor (14). Also of note is that the median holoTC concentrations in the two highest MMA quartiles (34 and 24 pmol/L) were both below the cutoff (35 pmol/L) used in other population groups (2, 15).

Consistent with previous reports, both Cbl and folate status influenced HCY in the currently investigated group (Fig. 1) (16, 17). The paradigm presented in Fig. 1 may justify concern about setting a recommended daily intake for folic acid or even a general reference range for folic acid in serum without considering Cbl status in different age ranges or socioeconomic groups (18). Our data confirm that the lowest HCY values may be achieved within the upper-normal range of serum folate when accompanied by better Cbl status (i.e., folic acid of 22–59 nmol/L and MMA of 84–181 nmol/L). The effect of moderately low Cbl status on HCY may be compensated for by higher folate status and vice versa (Fig. 1).

Taken together, our current study emphasizes the importance of both Cbl and folate status as determinants of HCY. Furthermore, the present work has important implications for public health. It seems prudent that folate requirements be defined in the light of Cbl status.

References