Biological Variation of Vitamins in Blood of Healthy Individuals

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Background: Components of biological variation can be used to define objective quality specifications (imprecision, bias, and total error), to assess the usefulness of reference values (index of individuality (II)), and to evaluate significance of changes in serial results from an individual (reference change value (RCV)). However, biological variation data on vitamins in blood are limited. The aims of the present study were to determine the intra- and interindividual biological variation of vitamins A, E, B1, B2, B6, C, and K and carotenoids in plasma, whole blood, or erythrocytes from apparently healthy persons and to define quality specifications for vitamin measurements based on their biology.

Methods: Fasting plasma, whole blood, and erythrocytes were collected from 14 healthy volunteers at regular weekly intervals over 22 weeks. Vitamins were measured by HPLC. From the data generated, the intra- (CVI) and interindividual (CVG) biological CVs were estimated for each vitamin. Derived quality specifications, II, and RCV were calculated from CVI and CVG.

Results: CVI was 4.8%–38% and CVG was 10%–65% for the vitamins measured. The CVIs for vitamins A, E, B1, and B2 were lower (4.8%–7.6%) than for the other vitamins in blood. For all vitamins, CVG was higher than CVI, with II <1.0 (range, 0.36–0.95). The RCVs for vitamins were high (15.8%–108%). Apart from vitamins A, B1, and erythrocyte B2, the imprecision of our methods for measurement of vitamins in blood was within the desirable goal.

Conclusions: For most vitamin measurements in plasma, whole blood, or erythrocytes, the desirable imprecision goals based on biological variation are obtainable by current methodologies. Population reference intervals for vitamins are of limited value in demonstrating deficiency or excess.

Adequate intake of vitamins is essential for normal growth and development and for the maintenance of health. Currently, the method of choice for assessing vitamin status in the laboratory is measuring their concentrations in plasma, whole blood, or erythrocytes (1–3). However, for most vitamins, objective quality specifications for such measurements have not been defined.

Several approaches to setting desirable quality specifications for imprecision and bias have been suggested (4–6), including reference interval–based goals, clinically based goals for imprecision, quality specifications laid down by external quality assurance (EQA)3 schemes, and biological variation–based goals. The European consensus is that quality specifications are best based on components of biological variation (7), but information on the biological variation of vitamins in blood is limited, apart from some studies on vitamins A and E and β-carotene (8–12).

The aims of this study were to determine the components of biological variation (intra- and interindividual) for fat-soluble (vitamins A, E, and K and carotenoids) and water-soluble (vitamins B1, B2, B6, and C) vitamins in plasma, erythrocytes, or whole blood of apparently healthy persons. Data on biological variation were used to define quality specifications (imprecision, bias, and total error) for measurements of vitamins in plasma, whole blood, or erythrocytes; to assess the usefulness of popu-

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Received June 20, 2005; accepted August 3, 2005.

Previously published online at DOI: 10.1373/clinchem.2005.056374

2 Nonstandard abbreviations: EQA, external quality assessment; TDP, thiamin diphosphate; PLP, pyridoxal 5-phosphate; Hb, hemoglobin; CV, intra-individual biological CV; SDx2, analytical variance; CVx, analytical CV; SDx2, total intra-individual variance; CVx, total intra-individual CV; SDx2, interindividual variance; SDx2, total variance; CVx, total CV; CVx, interindividual biological CV; II, index of individuality; and RCV, reference change value.
lation-based reference values; and to evaluate the significance of changes in serial results from an individual.

**Materials and Methods**

**PARTICIPANTS**

Fourteen apparently healthy members of the laboratory staff (7 males and 7 females; age range, 20–53 years) were recruited for this study. During the study period, all maintained their usual lifestyle, and none took any vitamin supplements or medications. The study was approved by the local ethics committee. All participants were informed of the purpose and procedure of the study, and all gave consent.

**SPECIMEN COLLECTION AND HANDLING**

Once every week for 22 weeks, plasma and blood were collected from each volunteer under standardized conditions to minimize sources of preanalytical variation. Fasting blood was obtained by conventional venipuncture between 0900 and 1000 in the morning with volunteers in a sitting position and avoiding venous stasis. The blood samples were collected into evacuated collection tubes containing either tripotassium EDTA or lithium heparin as anticoagulant (Greiner Bio-one) and protected from light. The blood samples were mixed by gentle rotation and inversion to prevent separation of plasma and cells, after which 1-mL aliquots of heparin- and EDTA-whole blood were removed to separate tubes and frozen at −70 °C. The remaining blood was centrifuged at 3000 g for 15 min within 2 h of collection. The plasma was removed, and packed erythrocytes were prepared by careful removal of all remaining plasma anduffy coat, aliquoted, and stored at −70 °C until analysis. For vitamin C analysis, aliquots of the heparin-plasma samples were stabilized with 60 g/L metaphosphoric acid (1:1 by volume) before storage.

**MEASUREMENT OF VITAMINS**

Vitamins were measured by HPLC. To minimize interbatch analytical variation, all samples from any given volunteer were assayed in a single batch for each of the analytes; therefore, for each vitamin measured, 14 different batches were run. The same lots of calibrators and quality-control materials were used throughout, and analyses were performed by a single analyst. Controls, treated in the same way as the samples, were analyzed in duplicate in each batch to generate analytical variation data. All samples were analyzed within 1 year of collection.

**VITAMINS A AND E AND CAROTENOIDS**

We assessed vitamin A (retinol), vitamin E (α-tocopherol), and carotenoid status by measuring their concentrations in plasma. Plasma retinol (vitamin A), α-tocopherol (vitamin E), and the carotenoids lutein, lycopene, α-carotene, and β-carotene were assayed by isocratic reversed-phase HPLC method using ultraviolet detection as described previously (13). Our laboratory uses plasma from a single donor, which is aliquoted and stored at −70 °C, as an in-house quality-control material for these analytes because a suitable commercial preparation is unavailable.

**VITAMIN K**

Phylloquinone (vitamin K₁) was measured in plasma as a marker of vitamin K status. The measurement in plasma was based on the method of Davidson and Sadowski (14). Briefly, vitamin K₁ was extracted from deproteinized plasma by solid-phase extraction and measured by reversed-phase HPLC with fluorescence detection after postcolumn reduction with platinum. Commercially available plasma-based quality-control material (Immundiagnostik AG) was used for assessing analytical variation. Triglyceride concentrations were measured in all samples that were analyzed for vitamin K.

**VITAMINS B₁, B₂, AND B₆**

Vitamin B₁, B₂, and B₆ status was determined by direct measurement of thiamin diphosphate (TDP), FAD, and pyridoxal 5-phosphate (PLP) in plasma, whole blood, or erythrocytes (1, 3, 15, 16).

Vitamin B₁. Because TDP is present almost exclusively in erythrocytes, vitamin B₁ status was assessed by measuring TDP in whole blood. TDP in whole blood was measured by HPLC using postcolumn ferricyanide derivatization and fluorometric detection as described previously (15). The TDP concentration in whole blood was related to hemoglobin (Hb) in the sample (ng TDP/g Hb). For the vitamin B₁ assay, analytical variation data were obtained by use of commercially available quality-control material (Chromsystems).

Vitamin B₂. FAD measurements in whole blood and erythrocytes were based on the method of Speek et al. (17). Briefly, whole blood or diluted hemolysates were precipitated with methanol and centrifuged, and the supernatant was injected for HPLC analysis. FAD was separated on an isocratic HPLC system with a reversed-phase C₁₈ column and fluorescence detection. We related FAD concentration in erythrocytes to Hb rather than to volume of packed cells because the viscosity of packed cells makes accurate pipetting difficult and, therefore, adversely affects the precision of the HPLC assay. For the erythrocyte vitamin B₂ assay, aliquots of packed erythrocytes from one donor, stored at −70 °C, were used as quality-control material. The quality control used in the assay for whole blood was a commercially available whole blood–based material (Chromsystems).

Vitamin B₆. PLP concentrations in plasma and erythrocytes were measured by HPLC using precolumn semicarbazide derivatization and fluorescent detection as described previously (16). For the reasons stated above, the PLP concentration in erythrocytes was related to Hb. For
the plasma assay, the control used was a commercially available plasma-based material (Chromsystems). For the erythrocyte assay, aliquots of packed erythrocytes from one donor, stored at −70 °C, were used as quality-control material.

VITAMIN C
Vitamin C status was assessed by measuring ascorbic acid in plasma. The measurement in plasma was based on the method of Margolis and Davis (18). Briefly, plasma stabilized and deproteinized with 60 g/L metaphosphoric acid was centrifuged, and an aliquot of the supernatant was injected on a C18 reversed-phase analytical column. After separation, the ascorbic acid was determined by electrochemical detection. Stabilized plasma from a single donor, aliquoted and stored at −70 °C, was used as an in-house quality-control material.

LIPIDS
Plasma cholesterol and triglycerides were measured according to the Lipid Research Clinics program protocol, standardized to the CDC (19).

PARTICIPATION IN EQA SCHEMES
Most of the HPLC assays used in this study have been evaluated in EQA schemes. We participated in and met the EQA scheme quality specifications for the following assays: (a) for vitamins A and E and carotenoids, the St. Heliers Hospital (Carshalton, Surrey, UK) and Instand EQA (Institut für Standardisierung und Dokumentation im medizinischen Laboratorium, Düsseldorf, Germany) schemes; (b) for vitamin K, the St. Thomas Hospital EQA (London, UK) scheme; (c) for vitamins B1, B2 (whole blood), and B6 (plasma), the Instand EQA scheme.

No EQA schemes exist for measurement of vitamins B2 and B6 in erythrocytes and vitamin C in plasma.

STATISTICAL ANALYSIS
Statistical analysis was carried with Minitab statistical software (release 13). Data for the vitamins measured in plasma, whole blood, or erythrocytes all followed a gaussian distribution as determined by the Shapiro–Wilk test. Outliers were determined as those exceeding ± 3 SD. After exclusion of any outliers, the data were analyzed to estimate components of biological variation. Correlations between variables were evaluated by the Pearson test. The intraindividual CVs (CVI) were compared by use of the F-test. A probability value (P) < 0.05 was set for statistical significance.

Analytical variance (SDA^2) was calculated from the difference between the duplicates according to the formula:

\[ SDA^2 = \frac{\sum d^2}{2N} \]

where d is the difference between duplicates, and N is the number of duplicates. The SDA^2 is expressed as relative SD (CV_A^2).

For each vitamin, total intraindividual variance (SDT^2I) was calculated from data for each participant and transformed into the total intraindividual CV (CV_I^2) by use of the homeostatic mean of each individual. Because CV_I^2 includes analytical and biological components, the CV_I for each participant was obtained by subtraction using the general formula (20):

\[ CV_I = (CV_T^2 - CV_A^2)^{1/2} \]

One half of the mean CV_I is proposed as the quality specification for precision (I); i.e., CV_A < 0.5 CV_I (7, 20).

The interindividual variance (SDG^2) reflects the difference between the means of the individuals and excludes intraindividual biological and analytical variation. To determine SDG^2, the total variance (SD^2) was calculated by use of all of the individual data sets and transformed to relative SD (CV_T) by use of the overall mean. The CV_I and CV_A were subtracted from CV_T to determine the interindividual biological CV (CV_C). Thus, from the formula described by Fraser and Harris (20):

\[ CV_C = (CV_T^2 - CV_I^2 - CV_A^2)^{1/2} \]

One fourth of the group biological variation, which itself is made up of intra- and interindividual variances, has been proposed as the limiting goal for bias (B); i.e., B < 0.25(CV_I^2 + CV_C^2)^{1/2} (7, 20).

The proposed quality specification for total error (TE) is to be less than kI + B, where k is 1.65 at \( \alpha = 0.05 \) (21). The index of individuality (II), which yields information about the utility of population-based reference intervals, was calculated as the ratio CV_T/TE (22, 23). The reference change value (RCV), which is the difference required for 2 serial measurements of the vitamin to have significantly changed at \( P < 0.05 \), was calculated as 2.77(CV_T) (20).

Results
The vitamin data showed a gaussian distribution (Shapiro–Wilk test); therefore, outliers were determined as those exceeding ± 3 SD. Of the 4620 data points, 17 were classified as outliers: 1 data point each for vitamin E/cholesterol, \( \alpha \)-carotene, \( \beta \)-carotene, vitamin B1, and erythrocyte vitamin B2; 2 data points each for lutein, vitamin K, vitamin K/triglycerides, whole blood vitamin B2, erythrocyte vitamin B6, and vitamin C. The overall means, medians, ranges, and the CV_I and CV_C are shown in Table 1. Because there were no significant differences in the CV_I and CV_C between the sexes (indicated by the F-test) for the vitamins investigated in this study, only the totals are presented. Also shown in Table 1 are the II and RCV, which are derived from biological variation data.

The ranges of CV_I values for the vitamins measured in the present study were wide, ranging from 4.8% to 38%. Vitamins A, E, B1, and B2 had relatively low CV_I values compared with the other vitamins. The CV_I values were similar for plasma and erythrocyte vitamin B6 (F = 1.3;
there was a significant positive correlation between vitamin K when corrected for triglycerides and not corrected for vitamin E when corrected for cholesterol and not CVI. As a result, their II values were less than CVI. Because in plasma vitamins E and K are transported mainly in LDL and VLDL, respectively, and their reference intervals have been shown to be influenced by the population lipid profile (24–26), we also obtained biological variation data for the vitamin E/cholesterol and vitamin K/triglyceride ratios. The CVI values were similar for vitamin E when corrected for cholesterol and not corrected for vitamin E (F = 1.2; P = 0.383) and for vitamin K when corrected for triglycerides and not corrected for vitamin K (F = 1.1; P = 0.439). As expected, there was a significant positive correlation between plasma concentrations of vitamin E and cholesterol (r = 0.68; P <0.001) and between vitamin K and triglycerides (r = 0.51; P <0.001).

For all of the vitamins listed in Table 1, CVG was higher than CVI. As a result, their II values were <1.0 (range, 0.36–0.95) with most being <0.6, the value below which population reference intervals are considered of limited value in demonstrating deficiency or excess (22, 23). The values for the RCV ranged from 15.8% to 108%.

For each vitamin, the imprecision of the laboratory method and the desirable specifications for imprecision (I), bias (B), and total error (TE) derived from the biological variation data are presented in Table 2. Apart from vitamins A, B, and erythrocyte B, the imprecision of our laboratory methods for measuring vitamin in plasma, whole blood, or erythrocytes was less than the desirable imprecision goals.

**Discussion**

The current European consensus is that quality specifications in laboratory medicine are best based on calculations involving biological variation (6, 7). Data on the biological variation of vitamins in blood are generally lacking. In this study, we generated biological variation data for vitamins that are commonly measured in the laboratory when assessing vitamin status. Using these data on components of biological variation, we have derived desirable quality specifications for measurement of vitamins in plasma, whole blood, or erythrocytes and assessed the usefulness of population-based reference intervals and the significance of changes in serial results obtained in an individual. Although the number of participants investigated in our study was small, a comparison of studies on biological variation demonstrates that estimates of intra- and interindividual variation are similar irrespective of the number of individuals studied (20, 27–29). Indeed, the CVI and CVG for vitamins A and E and β-carotene in plasma reported in the literature are similar to our values, suggesting that our results represent reliable estimates of biological variation (8–12).

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**Table 1. Components of biological variation, II, and RCV for vitamins in plasma, whole blood, or erythrocytes.**

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Units</th>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
<th>CVI, %</th>
<th>CVG, %</th>
<th>II</th>
<th>RCV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (retinol)</td>
<td>μmol/L</td>
<td>2.19</td>
<td>2.20</td>
<td>1.30–3.80</td>
<td>6.2</td>
<td>21</td>
<td>0.36</td>
<td>21.3</td>
</tr>
<tr>
<td>E (α-tocopherol)</td>
<td>μmol/L</td>
<td>32.4</td>
<td>31.0</td>
<td>19.2–56.0</td>
<td>7.6</td>
<td>21</td>
<td>0.37</td>
<td>21.9</td>
</tr>
<tr>
<td>E/Cholesterol</td>
<td>μmol/mmol</td>
<td>6.39</td>
<td>6.29</td>
<td>4.23–10.9</td>
<td>7.0</td>
<td>15</td>
<td>0.54</td>
<td>22.4</td>
</tr>
<tr>
<td>Lutein</td>
<td>μg/L</td>
<td>192</td>
<td>178</td>
<td>92.4–367</td>
<td>13</td>
<td>31</td>
<td>0.42</td>
<td>36.0</td>
</tr>
<tr>
<td>Lycopene</td>
<td>μg/L</td>
<td>196</td>
<td>196</td>
<td>42.0–435</td>
<td>22</td>
<td>33</td>
<td>0.69</td>
<td>63.4</td>
</tr>
<tr>
<td>α-Carotene</td>
<td>μg/L</td>
<td>47.2</td>
<td>39.7</td>
<td>10.3–191</td>
<td>24</td>
<td>65</td>
<td>0.38</td>
<td>69.2</td>
</tr>
<tr>
<td>β-Carotene</td>
<td>μg/L</td>
<td>276</td>
<td>259</td>
<td>67.2–748</td>
<td>18</td>
<td>48</td>
<td>0.38</td>
<td>49.3</td>
</tr>
<tr>
<td>K (phyloquinone)</td>
<td>nmol/L</td>
<td>1.59</td>
<td>1.45</td>
<td>0.21–6.50</td>
<td>38</td>
<td>44</td>
<td>0.88</td>
<td>108</td>
</tr>
<tr>
<td>K/Triglycerides</td>
<td>nmol/mmol</td>
<td>1.85</td>
<td>1.32</td>
<td>0.23–4.14</td>
<td>30</td>
<td>46</td>
<td>0.72</td>
<td>90.7</td>
</tr>
<tr>
<td>B2 (TDP)</td>
<td>ng/g Hb</td>
<td>501</td>
<td>486</td>
<td>361–775</td>
<td>4.8</td>
<td>12</td>
<td>0.47</td>
<td>15.8</td>
</tr>
<tr>
<td>Whole blood B2 (FAD)</td>
<td>nmol/L</td>
<td>384</td>
<td>377</td>
<td>252–554</td>
<td>5.8</td>
<td>10</td>
<td>0.59</td>
<td>17.1</td>
</tr>
<tr>
<td>Erythrocyte B2 (FAD)</td>
<td>nmol/g Hb</td>
<td>2.33</td>
<td>2.15</td>
<td>1.13–4.61</td>
<td>6.4</td>
<td>11</td>
<td>0.75</td>
<td>25.5</td>
</tr>
<tr>
<td>Plasma B6 (PLP)</td>
<td>nmol/L</td>
<td>52.9</td>
<td>51.1</td>
<td>23.1–155</td>
<td>20</td>
<td>34</td>
<td>0.61</td>
<td>58.0</td>
</tr>
<tr>
<td>Erythrocyte B6 (PLP)</td>
<td>nmol/g Hb</td>
<td>354</td>
<td>349</td>
<td>191–740</td>
<td>14</td>
<td>24</td>
<td>0.60</td>
<td>41.4</td>
</tr>
</tbody>
</table>

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**Table 2. Laboratory method imprecision (CVI) and desirable specifications for imprecision, bias, and total error derived from biological variation data.**

<table>
<thead>
<tr>
<th>Desirable specification</th>
<th>Vitamin</th>
<th>I* %</th>
<th>B, %</th>
<th>TE, %</th>
<th>CVI, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>3.2</td>
<td>5.4</td>
<td>10.7</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>3.8</td>
<td>5.6</td>
<td>11.9</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>E/Cholesterol</td>
<td>3.5</td>
<td>4.1</td>
<td>9.9</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>Lutein</td>
<td>6.5</td>
<td>8.5</td>
<td>19.2</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>Lycopene</td>
<td>11.2</td>
<td>9.9</td>
<td>28.1</td>
<td>5.4</td>
<td></td>
</tr>
<tr>
<td>α-Carotene</td>
<td>12.0</td>
<td>17.4</td>
<td>36.8</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>β-Carotene</td>
<td>9.1</td>
<td>12.9</td>
<td>27.9</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>K</td>
<td>19.3</td>
<td>14.6</td>
<td>45.9</td>
<td>9.0</td>
<td></td>
</tr>
<tr>
<td>K/Triglycerides</td>
<td>15.2</td>
<td>13.8</td>
<td>38.6</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>B2 (whole blood)</td>
<td>2.4</td>
<td>3.1</td>
<td>7.1</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>B2 (erythrocytes)</td>
<td>2.9</td>
<td>3.0</td>
<td>7.8</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>B2 (plasma)</td>
<td>3.2</td>
<td>4.3</td>
<td>9.6</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>B6 (erythrocytes)</td>
<td>10.1</td>
<td>9.8</td>
<td>26.3</td>
<td>3.6</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>8.8</td>
<td>6.8</td>
<td>18.0</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td>10.0</td>
<td>7.2</td>
<td>23.7</td>
<td>3.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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* I, imprecision; B, bias; TE, total error.
Compared with other vitamin, the $CV_i$ values for vitamins A, B1, and B2 were relatively low (<8%), indicating relatively tight homeostatic control in an individual for these vitamins. Although vitamin B2 and B6 status is usually assessed by measuring FAD in whole blood and PLP in plasma, respectively, recent evidence suggests that their concentrations in erythrocytes may more reliably reflect tissue stores, particularly in the presence of systemic inflammation (30–33). We therefore also generated biological variation data for FAD and PLP in erythrocytes.

In the present study the desirable goal for imprecision was easily achieved in our laboratory for 12 of the 15 vitamins investigated. Exceptions were measurements of plasma retinol (vitamin A), whole blood TDP (vitamin B1), and erythrocyte FAD (vitamin B2). The ideal quality-control material to derive data for such laboratory imprecision would have the same matrix as the sample on which the analysis is to be carried out. This was true for vitamins A and E, carotenoids, erythrocyte B2, erythrocyte B6, and vitamin C, for which we used in-house quality-control materials (plasma or erythrocytes from a single donor). In contrast, commercially prepared human blood–based quality-control material was used for vitamins K and B4, whole blood B2, and plasma B6. For these vitamins, the CVs obtained with the commercial quality-control materials were 9.0%, 3.0%, 2.1%, and 3.6%, respectively, which were similar to those for our in-house quality-control materials (8.4%, 3.2%, 2.5%, and 3.9%, respectively; $n = 22$, from recent routine between-batch analysis over a period of 4 months (D.K. Talwar, unpublished data)); therefore, the sample matrix would appear not to be a significant confounding factor in the present study.

Using the biological variation data, we documented the desirable total error goal for vitamin measurements in plasma, whole blood, or erythrocytes. It has been proposed that EQA schemes use total error based on biology for describing the maximum allowable error for single determinations of quality-control materials (21); however, at present, none of the EQA schemes for vitamin measurements in plasma, whole blood, or erythrocytes use this approach.

Reference intervals for vitamins are usually based on the mean and SD of a population sample, but these reference intervals are useful for making decisions only when $CV_i$ is greater than $CV_C$. The II, which is the ratio between $CV_i$ and $CV_C$, indicates the degree to which a single measurement in the population is able to distinguish an unusual result for an individual (22, 23). When the II is <0.6, an isolated result compared with the population-based reference interval is considered to have little diagnostic value although it may be useful for monitoring. In contrast, when the II is >1.4, an isolated result could be compared usefully with reference values for diagnosis. In our study, the $CV_i$ was less than the $CV_C$ for all vitamins studied, with II values <1.0. Thus, for vitamins, reference intervals based on population studies will be of limited value in demonstrating deficiency or excess.

The RCVs for the vitamins were relatively high, mainly because of their large within-subject variations. This means that relatively large differences between the results of sequential samples would be required for them to be significantly different ($P < 0.05$) (20).

In summary, we have calculated quality specifications for vitamin measurements in plasma, whole blood, or erythrocytes based on the biological variation. For most vitamin measurements, desirable imprecision is easily obtained by current methodologies. Conventional reference intervals for vitamins are of limited value in the detection of unusual results for a particular individual.

References


