Reference Intervals for Blood Ammonia in Healthy Subjects, Determined by Microdiffusion

To the Editor:

The determination of blood ammonia concentration is important for the diagnosis and follow-up of several hepatic and renal pathologies in adult and pediatric patients and newborns (1, 2). Ammonia can be measured by several methods (1, 3, 4). The reported reference intervals for ammonia concentrations vary widely, at least in part, because of technical pitfalls (4), problems related to the sampling (1, 3), the time required for analysis, and limitations specific for each method—which make it difficult to choose the best method. Moreover, reference intervals vary with age and sex of the subjects and type of sample (1, 3–5). Our aim was to establish blood ammonia reference intervals in our healthy population, in children and adults, by a microdiffusion method (Ammonia Checker II; Menarini Diagnostics, Firenze, Italy). The ammonia ion in the specimen is converted by an alkaline buffer agent (borate buffer) to ammonia gas, which is liberated from the blood sample, passes through the pores of spacer, and reaches the indicator (bromcresol green) to cause color development. Because the color development is proportional to the concentration of ammonia gas produced, the blood ammonia concentration is quantitatively determined by measuring the color developed.

With the consent of our hospital’s Clinical Research Committee we measured blood ammonia in 400 ambulatory subjects selected for absence of known organic disease. To further check their state of health, we subjected them to a conventional biochemical screening and hematological analysis. The study groups were: group A, newborns, <30 days; group B, infants, 1 month to 1 year; group C, children, 1 year to 14 years; and group D, people >14 years old classified in two subgroups—group D1 (men) and group D2 (women). For each group, we selected a representative sample as a reference population, according to the IFCC guidelines (6, 7). From the initial 100 individuals in each group, we discarded the results of those who, in the diagnosis, had some disease and more than one biochemical measurement altered. All blood specimens were obtained by venipuncture, collected with EDTA/K3 as anticoagulant, placed on ice, and analyzed within 5 min. For each population group, the distribution of ammonia concentration values was such that, in each group, the blood ammonia values followed a gaussian frequency distribution, as verified by the Kolmogorov–Smirnov test. Aberrant values were excluded according to the IFCC guidelines (6).

In group D, the composite distribution was not significantly different from the distribution for either sex separately. Accordingly, we calculated both parametric (mean ± 2SD) and nonparametric (0.05–0.95 fractiles) reference intervals (Table 1). Blood ammonia concentration decreased with age (P < 0.05), except in group D, in which ammonia increased (P < 0.05). This increase is higher in men than in women. Our results are somewhat higher than those from other studies performed with other methods (1, 4, 5).

References

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Can Hematology Reference Intervals Be Derived from Hospitalized Patients’ Data?

To the Editor:

We read with great interest the paper of Kouri et al. (1), which described an attempt to derive useful reference intervals for hemoglobin, mean corpuscular volume (MCV), and red blood cell (RBC; erythrocyte) count from hospitalized patients’ data. If proved reliable, this approach would be a boon to the laboratorian, given the huge amounts of effort that must be expended to derive valid gender- and age-related hematology reference intervals. We were puzzled, however, by certain inconsistencies in the reference intervals of Kouri et al. and concluded that the authors should have validated their reference intervals. Validation is most easily performed by comparing the authors’ reference intervals with previously established intervals.

Hematology reference intervals for healthy, well-nourished populations

Table 1. Reference intervals for blood ammonia concentration (µmol/L). Reference intervals

<table>
<thead>
<tr>
<th>Age</th>
<th>n</th>
<th>Mean</th>
<th>Mean ± 2SD</th>
<th>0.05–0.95 fractiles</th>
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</thead>
<tbody>
<tr>
<td>&lt;30 days</td>
<td>87</td>
<td>54.0</td>
<td>17–91</td>
<td>21–95</td>
</tr>
<tr>
<td>1–12 months</td>
<td>91</td>
<td>43.5</td>
<td>15–72</td>
<td>19–74</td>
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<tr>
<td>1–14 years</td>
<td>94</td>
<td>39.5</td>
<td>14–65</td>
<td>17–68</td>
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<tr>
<td>&gt;14 years</td>
<td>182</td>
<td>41.0</td>
<td>18–64</td>
<td>22–66</td>
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<tr>
<td>Men</td>
<td>89</td>
<td>43.5</td>
<td>19–68</td>
<td>21–71</td>
</tr>
<tr>
<td>Women</td>
<td>93</td>
<td>38.5</td>
<td>17–60</td>
<td>19–63</td>
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