Harmonisation of Reference Intervals

In recent times it has become clear to the users and commissioners of hospital diagnostic services that there are differences in reference intervals and units of measurement between laboratories. We, in the profession, recognise that there are sometimes genuine scientific reasons for these differences, for example differences in local populations or analytical methodology. However, it is important to differentiate those analytes for which there is no clearly identifiable reason for a difference. It is these analytes that have been considered by the Pathology Harmony group. This is a professionally led group supported by a grant from the Department of Health.

The identification of harmonisable analytes has been achieved through a process of consensus involving a large number of laboratory scientists supported by professional bodies. Clearly many analytes, particularly those measured by immunoassay, cannot be easily harmonised. This has been recognised by Pathology Harmony and further work will be necessary. In addition, this group has made recommendations on units of measurement that should be used to minimise possibility of confusion.

The Association for Clinical Biochemistry, the Institute of Biomedical Science and Royal College of Pathologists support this process and believe that the introduction of common reference ranges and units of measurement will improve patient safety.

We recommend that our members should introduce these changes and would hope that this can be achieved by April 2011.

Julian Barth
President, Association for Clinical Biochemistry

James Kenneth Rae
President, Institute of Biomedical Science

Danielle Freedman
Chair, SAC Clinical Biochemistry and Vice-President, Royal College of Pathologists
<table>
<thead>
<tr>
<th>Test Name</th>
<th>Units</th>
<th>Range low</th>
<th>Range high</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>mmol/L</td>
<td>133</td>
<td>146</td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td>mmol/L</td>
<td>3.5</td>
<td>5.3</td>
<td></td>
</tr>
<tr>
<td>Urea</td>
<td>mmol/L</td>
<td>2.5</td>
<td>7.8</td>
<td></td>
</tr>
<tr>
<td>Chloride</td>
<td>mmol/L</td>
<td>95</td>
<td>108</td>
<td></td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>mmol/L</td>
<td>22</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Phosphate</td>
<td>mmol/L</td>
<td>0.8</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td>mmol/L</td>
<td>0.7</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>g/L</td>
<td>35</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Total Protein</td>
<td>g/L</td>
<td>60</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>Osmolality</td>
<td>mmol/kg</td>
<td>275</td>
<td>295</td>
<td></td>
</tr>
<tr>
<td>Alkaline Phosphatase (ALP)</td>
<td>U/L</td>
<td>30</td>
<td>130</td>
<td>IFCC candidate method p-NPP using AMP buffer</td>
</tr>
<tr>
<td>Creatine Kinase (CK)</td>
<td>U/L</td>
<td>40</td>
<td>320 (M)</td>
<td>Ranges are for white Caucasian only; other ethnic groups may have higher values</td>
</tr>
<tr>
<td>Bilirubin (total)</td>
<td>µmol/L</td>
<td>&lt;21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted Calcium</td>
<td>mmol/L</td>
<td>2.2</td>
<td>2.6</td>
<td>Use adjustment equations normalised to mean calcium of 2.4 mmol/L</td>
</tr>
<tr>
<td>Urate</td>
<td>µmol/L</td>
<td>200</td>
<td>430 (M)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>140</td>
<td>360 (F)</td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>mg/L</td>
<td>4</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>mg/L</td>
<td>10</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Phenytoin</td>
<td>mg/L</td>
<td>5</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Theophylline</td>
<td>mg/L</td>
<td>10</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Valproate</td>
<td>mg/L</td>
<td></td>
<td>No range should be quoted</td>
<td></td>
</tr>
<tr>
<td>Paracetamol</td>
<td>mg/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salicylate</td>
<td>mg/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>µmol/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lithium</td>
<td>mmol/L</td>
<td>0.4</td>
<td>1.0</td>
<td>Complies with NPSA guidance</td>
</tr>
<tr>
<td>Digoxin</td>
<td>µg/L</td>
<td>0.5</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>µg/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25OH Vitamin D (including separately measured D2 &amp; D3)</td>
<td>nmol/L</td>
<td>No ranges recommended</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTH</td>
<td>pmol/L</td>
<td></td>
<td>Method dependent</td>
<td></td>
</tr>
<tr>
<td>BNP/NTproBNP</td>
<td>ng/L</td>
<td></td>
<td>Method dependent</td>
<td></td>
</tr>
<tr>
<td>Troponin I</td>
<td>ng/L</td>
<td></td>
<td>Method dependent</td>
<td></td>
</tr>
<tr>
<td>Troponin T</td>
<td>ng/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 h Urine Calcium</td>
<td>mmol/24h</td>
<td>2.5</td>
<td>7.5</td>
<td></td>
</tr>
<tr>
<td>24 h Urine Urate</td>
<td>mmol/24h</td>
<td>1.5</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>24 h Urine Phosphate</td>
<td>mmol/24h</td>
<td>15</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>24 h Urine Magnesium</td>
<td>mmol/24h</td>
<td>2.4</td>
<td>6.5</td>
<td></td>
</tr>
</tbody>
</table>
## Agreed Paediatric Clinical Biochemistry Reference Intervals

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Age</th>
<th>Units</th>
<th>Range low</th>
<th>Range high</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>No age-related differences</td>
<td>mmol/L</td>
<td>133</td>
<td>146</td>
<td></td>
</tr>
<tr>
<td>Plasma Potassium</td>
<td>Neonate</td>
<td>mmol/L</td>
<td>3.4</td>
<td>6.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infant</td>
<td>mmol/L</td>
<td>3.5</td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-16 yrs</td>
<td>mmol/L</td>
<td>3.5</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>Urea</td>
<td>Neonate</td>
<td>mmol/L</td>
<td>0.8</td>
<td>5.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infant</td>
<td>mmol/L</td>
<td>1.0</td>
<td>5.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-16 yrs</td>
<td>mmol/L</td>
<td>2.5</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td>Neonate</td>
<td>mmol/L</td>
<td>0.6</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infant - 16 yrs</td>
<td>mmol/L</td>
<td>0.7</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Plasma lactate</td>
<td>No age-related differences</td>
<td>mmol/L</td>
<td>0.6</td>
<td>2.5</td>
<td>Enzymatic method only</td>
</tr>
<tr>
<td>Bilirubin (total)</td>
<td>14 days - 16 yrs</td>
<td>µmol/L</td>
<td>&lt;21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>Neonate</td>
<td>g/L</td>
<td>30</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infant</td>
<td>g/L</td>
<td>30</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-16 yrs</td>
<td>g/L</td>
<td>30</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>Neonate</td>
<td>mmol/L</td>
<td>2.0</td>
<td>2.7</td>
<td>Actual not adjusted</td>
</tr>
<tr>
<td></td>
<td>Infant - 16 yrs</td>
<td>mmol/L</td>
<td>2.2</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>Phosphate</td>
<td>Neonate</td>
<td>mmol/L</td>
<td>1.3</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infant</td>
<td>mmol/L</td>
<td>1.3</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-16 yrs</td>
<td>mmol/L</td>
<td>0.9</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Alkaline Phosphatase (ALP)</td>
<td>Neonate</td>
<td>U/L</td>
<td>70</td>
<td>380</td>
<td>p-NPP using AMP buffer</td>
</tr>
<tr>
<td></td>
<td>Infant - 16 yrs</td>
<td>U/L</td>
<td>60</td>
<td>425</td>
<td></td>
</tr>
<tr>
<td>Ammonia</td>
<td>Sick or premature</td>
<td>µmol/L</td>
<td>&lt;150</td>
<td></td>
<td>Follow metbio.net guidance</td>
</tr>
<tr>
<td></td>
<td>Neonate</td>
<td>µmol/L</td>
<td>&lt;100</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infant - 16 yrs</td>
<td>µmol/L</td>
<td>&lt;50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma Bicarbonate</td>
<td>No age-related differences</td>
<td>mmol/L</td>
<td>19</td>
<td>28</td>
<td></td>
</tr>
</tbody>
</table>

Definitions: Neonate <4 weeks; Infant 4 weeks – 1 year

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**What Happens Next . . .**

The Pathology Harmony project was conceived as an action learning set in the West Midlands SHA and more recently has received support from Dr Ian Barnes and the Department of Health. In Phase II of the project laboratory staff were joined by representatives from the Royal College of Pathologists, Association for Clinical Biochemistry and Institute of Biomedical Science.

The results of Phase I and II of the project have culminated in recommendations that have been widely consulted on, including consideration by professional groups. Phase II of this work included studies in Immunology and Haematology but here we present just the harmonised reference intervals and units in Clinical Biochemistry.

Details of the members of Pathology Harmony group and approaches taken and background information behind the decisions that are presented here can be found on the Pathology Harmony website.

**What Next?**

Early in 2011 the Pathology Harmony group will be meeting to consider how to take forward new areas of activity. If you have comments or suggestions then you can contact Pathology Harmony by emailing: secretary@pathologyharmony.co.uk