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Letter to the Editor

Common reference intervals of blood counts

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On behalf of the Working Group Guide Limits of the DGKL (German Society for Clinical Chemistry and Laboratory Medicine)

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The highest degree of interlaboratory comparability of examination results can presently be achieved by the International Federation of Clinical Chemistry (IFCC) reference system including reference materials, reference procedures, reference laboratories, and reference limits. Because the IFCC recommendations for establishing reference limits cannot be fulfilled by most routine laboratories, several authors have advocated the determination of common reference intervals by multicentre studies [1, 2]. Nebe et al. [3] recently published a useful multicentre study on reference intervals of blood counts. Nine centres participated with different analytical systems. One system was identical in all laboratories. The authors did not combine their reference limits to common limits, but only for single systems. Statistical justifications, as, for example, the test proposed by Lahti et al. and Gellerstedt and Petersen [4, 5], for combining the limits obtained from the various laboratories, were not presented. Although all analytical systems were CE-marked and from leading manufacturers, distinct differences were reported. For example, at the upper reference limit (97.5th percentile) for haemoglobin, the difference between the highest and lowest value was 12.0 g/L, corresponding to 33% of the mean reference range[1] (females). For RDW (distribution of erythrocyte volume) the difference between the highest and lowest value was 96% of the mean reference range, reticulocytes 31% (males), thrombocytes 37% (males), leucocytes 23% (females), monocytes 60% (males), eosinophile granulocytes 94% and basophile granulocytes 177%. In our experience, a difference >20% of the reference range is critical. The statistical significance of the differences mentioned remains unknown because the authors did not report which statistical criteria they applied. However, the permissible limit for proficiency testing for example, haemoglobin is 6% according to the national guideline [6]. Therefore, we understand that the authors did not combine their results for common reference intervals.

The authors advocated system-specific reference intervals for some quantities, and intra-laboratory intervals for some critical quantities. This plea is in complete agreement with the recommendations of the working group "guide limits" ("Richtwerte") of the German Society for Clinical Chemistry and Laboratory Medicine (DGKL). The working group has published a statistical approach to derive intra-laboratory reference limits from retrospective large data bases stored in laboratory information systems [7, 8]. This approach is currently being further improved.

We also support the plea of Nebe et al. [3] that the source of reference intervals must be identified by accredited laboratories. We would like to add that laboratories should prepare a written policy document on how they adopt reference limits and how they periodically review their limits according to ISO 15189.

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[1]The terms reference range and reference interval are often used interchangeably. Reference interval is defined by a lower and an upper reference limit (e.g., for potassium in serum: from 3.6 to 5.0 mmol/L, abbreviated as 3.6–5.0), whereas reference range is defined by only one single value which is the difference between the upper and the lower reference limit (1.4 mmol/L for potassium). The reference range may also be called span of the reference interval [9].

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