

# The importance of determining reference intervals for Laboratory Medicine

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Exactly 20 years ago, Forsman has shown that at least 70% of clinical decisions made within hospital setting were very dependent on the results of laboratory tests<sup>(1)</sup>. Nowadays, with the remarkable technological evolution, probably this contributory percentage is even higher.

The performance of a laboratory test may have different purposes such as the diagnosis of a particular disease, monitoring a patient undergoing a therapeutic regimen, the staging of a disease already diagnosed or risk prediction for a particular, among other reasons. With the purpose that the result can be correctly interpreted and, therefore be useful in the medical practice, it needs to fulfill some requirements, such as having been obtained by reliable and robust methodology, have positive and negative predictive values relevant, and high levels of sensitivity and specificity<sup>(2,3)</sup>. Additionally, it is essential that their limits of significance and limitations are well known, which means, it is crucial to have their reference intervals well determined<sup>(4)</sup>.

The World Health Organization (WHO), the International Federation for Clinical Chemistry (IFCC) and the Clinical Laboratory Standard Institute (CLSI) define reference interval as the set of results obtained by observation or quantitative measurement of an analyte in a selected group of individuals, based on well-defined criteria<sup>(5)</sup>.

In the United States of America, since 1988 there are regulatory standards on how clinical laboratories should create and evaluate, periodically, the reference intervals adopted<sup>(6)</sup>. In Brazil, the legislation (RDC 302) of the Agência Nacional de Vigilância Sanitária (Anvisa)<sup>(7)</sup> and the Programa de Acreditação de Laboratórios Clínicos (PALC) of the Sociedade Brasileira de Patologia Clínica/Medicina Laboratorial (SBPC/ML) only determine that all clinical laboratory should provide some reference value with the test result. Thus, it is granted to the laboratory to set its own intervals, validate the values provided by the manufacturer of the supplies, or even adopt the values available in the literature. Clearly, determining their own reference intervals, although very desirable, is more laborious and costly than the other options because it entails literature review, selection of reference individuals, application of detailed questionnaires, and analysis of biological variables, such as gender, age and genetic variability, among other tasks. Furthermore, the characteristics of the population in which the reference range was determined and the population to which it is applied must be compatible<sup>(8)</sup>. For the pediatric population, the difficulties may be even greater, but there is a number of studies on the determination of reference intervals<sup>(9-12)</sup>; regarding the geriatric population, the data are still scarce or outdated<sup>(13, 14)</sup>. Data submitted by the College of American Pathologists (CAP) in a interlaboratory study involving 163 clinical laboratories, with special focus on the origin of the reference intervals used, showed that for the adult population approximately 50% of laboratories used their own reference intervals, but when the pediatric population was assessed, this percentage decreased to 25%<sup>(15)</sup>. Thus, it is with great enthusiasm that we observe some research centers get involved in this subject, as demonstrated in the publication of this issue of the *Jornal Brasileiro de Patologia e Medicina Laboratorial (JBPMML)*, in the study of Cruz *et al.* (2016) "Reference intervals of amino acids by high performance liquid chromatography in plasma samples of Brazilian children"<sup>(16)</sup>.

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## REFERENCES

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