

## EDITORIAL:

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### *eJIFCC SPECIAL ISSUE ON LABORATORY REFERENCE INTERVALS*

Recent decades have witnessed a tremendous increase in the number of new diagnostic methods and the introduction of many emerging new biomarkers in clinical diagnostic laboratories. The utility of biomarkers as screening and diagnostic tools is limited by many factors, such as sensitivity, specificity and predictive values. Another critical factor, not always carefully considered, is the availability of appropriate reference intervals that allow appropriate interpretation of results from tested individuals. In order for reference intervals to be available, it requires access to human biological specimens from healthy individuals (with the associated uncertainties on the definition of health in that context). Ideally, reference intervals should be determined by sampling a healthy population that span the whole age range and include both genders. Furthermore, since many reference intervals are being defined as dependent on several anthropometric parameters, optimal reference intervals should be established based on gender, ethnicity, age when pre-assessment of results revealed inter-dependency. Access to healthy individuals represents one major challenge for hospital-based clinical laboratories, since the vast majority of samples are drawn from hospitalized or clinic patients that are likely to suffer from clinical or sub-clinical disease and not truly represent a normal population. This challenge is particularly apparent with dealing with specific populations such as pediatrics or geriatrics.

Diagnosis and monitoring of almost all pediatric diseases require the measurement of a wide range of disease biomarkers with varying degree of clinical specificity and sensitivity. These biomarkers are commonly measured in clinical laboratories and the results interpreted based on established reference (or normal) intervals. In order to validate a marker for use in the diagnosis of clinical disorders, the hormones or chemical substances must be measured in large normal populations of various ages, ethnicities and both genders. Once the reference intervals for healthy subjects are determined, the test can then be used more accurately for the diagnosis of clinical disorders. There is ample evidence in the medical literature that appropriate diagnosis of pediatric disease requires the use of age appropriate reference intervals and careful consideration of gender differences and variations related to ethnic origin. With the increasing diversity of the world population, there is clearly a critical need to establish meaningful pediatric reference intervals that can be used across populations and regions. Considering these serious gaps, many obvious questions arise including: What is the value of a lab test result without appropriate interpretation?? What are the risks of using outdated, inaccurate, and inappropriate reference intervals?? Why are clinical laboratories and industry ignoring the issue?? Can we afford to ignore the issue much longer?? The critical gaps in the available laboratory reference intervals have the clear potential of contributing to delays in diagnosis of many diseases in both children and adults. It is thus critical and of utmost urgency that more acceptable and comprehensive databases are established in these populations.

The current gaps in both adult and paediatric reference intervals and approaches to development of new reference intervals are the focus of five publications in this edition of the eJIFCC Journal. The topics covered in this issue are Practical Aspects of Reference Interval Determination by Gary L. Horowitz, Reference Intervals and Decision Limits by Ferruccio Ceriotti and Joseph Henney, the CALIPER Initiative on Paediatric Reference Intervals by Adeli and colleagues, Biochemical Markers of Bone Health in Childhood by Grey and colleagues, and Accurate Reference Intervals by Aytakin and Emerk. *The Editorial Board of eJIFCC is pleased to feature these articles in the September 2008 issue of the journal.*

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