Clinical Chemistry

August 2015 Audio Summary

This is the August 2015 issue of *Clinical Chemistry*, Volume 61, Issue 8.

On the cover this month: The kilogram and the tape measure. For millennia, man has attempted to develop reference standards for weight, length, and time. The grain (for measuring precious metals) gave way to the stone (for measuring body weight), which has been replaced by the pound and the kilogram (the current international standard). For measures of distance, the cubit (length from elbow to fingertips) gave way to the span (width of spread fingers), which has been replaced by the inch and the meter (the current international standard). Today, clinical laboratories seek accuracy and consistency through harmonization and commutability efforts. For optimal test results interpretation, we seek to define appropriate reference intervals. This month's issue of *Clinical Chemistry* contains 3 articles and 2 editorials dealing with the establishment of reference intervals for biochemical, endocrine and hematologic markers across pediatric, adult, and geriatric ages. Also in this issue is an article describing an approach for commutability assessment of HDL and LDL cholesterol.

**Biochemical Marker Reference Values across Pediatric, Adult, and Geriatric Ages: Establishment of Robust Pediatric and Adult Reference Intervals on the Basis of the Canadian Health Measures Survey**
By Khosrow Adeli, et al.

Age and gender can significantly influence biomarker reference values, however, there has been no comprehensive examination of such changes across pediatric, adult, and geriatric groups. Statistics Canada's Canadian Health Measures Survey collected blood and health information from approximately 12,000 Canadians aged 3-79 years and measured 24 biochemical markers using the Ortho Vitros 5600 FS analyzer. CALIPER has collaborated with Statistics Canada to develop age- and sex-stratified reference intervals for these biomarkers, in accordance with Clinical and Laboratory Standards Institute C28-A3 guidelines. Reference intervals revealed dynamic changes in biochemical marker levels over the age range, and will provide important clinical information for monitoring disease states.

**Complex Reference Values for Endocrine and Special Chemistry Biomarkers across Pediatric, Adult, and Geriatric Ages: Establishment of Robust Pediatric and Adult Reference Intervals on the Basis of the Canadian Health Measures Survey**
By Khosrow Adeli, et al.

Accurate reference intervals are critical to interpret laboratory test results. Existing reference intervals are currently out-of-date or are based on unhealthy populations. The Canadian Health Measures Survey collected blood and health information from the Canadian household population, and with the Canadian Laboratory Initiative on Pediatric Reference Intervals program, has established age- and sex-specific reference intervals for 13 immunochemical biomarkers. Biomarker levels fluctuated throughout the age range and gender partitioning was required for 4 analytes. This study enables a detailed examination of immunochemical marker changes that occur in healthy individuals, provides insight into complex biological changes throughout development and aging, and will contribute to improved clinical test interpretation.

**Complex Biological Profile of Hematologic Markers across Pediatric, Adult, and Geriatric Ages: Establishment of Robust Pediatric and Adult Reference Intervals on the Basis of the Canadian Health Measures Survey**
By Khosrow Adeli, et al.

Accurate reference intervals for hematological markers are either outdated or unavailable. CALIPER has collaborated with the Canadian Health Measures Survey to develop a comprehensive database of reference intervals in a large population of Canadian children and adults aged 7 to 79 years. Blood samples were collected from 12,000 healthy Canadians before analysis of 16 markers and calculation of reference intervals. Reference value distributions showed dynamic changes from childhood into adulthood and between genders, necessitating distinct partitions throughout life. This robust dataset has allowed observation of dynamic biological profiles and resulted in the establishment of comprehensive age- and sex-specific reference intervals that may contribute to improved patient monitoring.

**Influence of Glycosylation on Diagnostic and Prognostic Accuracy of N-Terminal Pro–B-Type Natriuretic Peptide in Acute Dyspnea: Data from the Akershus Cardiac Examination 2 Study**
By Helge Røsjø, et al.

Previous studies have demonstrated that the N-terminal part of pro-B-type natriuretic peptide or NT-proBNP is glycosylated, but whether glycosylation influences the diagnostic and prognostic accuracy of NT-proBNP measurements is not known. This study presents data on NT-proBNP measurements in 309 patients with acute dyspnea performed in standard EDTA tubes and in EDTA tubes pre-treated with deglycosylation enzymes. The authors found that NT-proBNP measurements were higher and their diagnostic and prognostic accuracy seemed to be improved by pre-treating tubes with deglycosylation enzymes. Accordingly, deglycosylation of NT-proBNP may provide an approach to enhance the diagnostic and prognostic value of the current gold standard biomarker of heart failure.

**Tumor MicroRNA Expression Profiling Identifies Circulating MicroRNAs for Early Breast Cancer Detection**
By Nerea Matamala, et al.

Given their important role in tumorigenesis and remarkable stability in body fluids, microRNAs are promising biomarkers. By using 2 series of formalin fixed paraffin embedded breast tumors and two series of plasma, the authors have identified 4 microRNAs that are deregulated both in tumors and plasma from patients with breast cancer when compared with healthy individuals. The expression levels of 2 of them (miR-505-5p and miR-96-5p) have not been associated with breast cancer before and have the highest discrimination capability. The identified microRNAs have potential utility in early breast cancer detection and surveillance.

**Difference in Bias Approach for Commutability Assessment: Application to Frozen Pools of Human Serum Measured by 8 Direct Methods for HDL and LDL Cholesterol**

By William J. Korzun, et al.

A new approach to evaluate commutability based on the difference in bias between patient samples and reference materials was used to evaluate 4 frozen off-the-clot serum pools intended for use to assess calibration traceability. When medical use criteria were applied, 1 of 4 pools was found to be commutable with patient specimens for 8 direct HDL cholesterol methods, and none of the pools was commutable for 8 direct LDL cholesterol methods. When criteria based on random error components were used, all pools were commutable for HDL and 1 of 4 was commutable for LDL cholesterol methods.