Clinical Chemistry

May 2015 Audio Summary

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On the cover this month: *Girl Before a Mirror* by Pablo Picasso. This 1932 painting shows Picasso's mistress Marie-Thérèse Walter, one of his favorite subjects. The image itself can be interpreted in many ways, but many scholars see a woman looking at her own mortality in the mirror; a future of old age, loss of vitality, physical inability, and disease. Although both men and women face these same challenges, some diseases and their conditions are unique to women, such as complications of pregnancy. This issue of *Clinical Chemistry* contains a Q&A on preeclampsia, an old disease with new tools for better diagnosis and risk management. This month's Clinical Case Study and What Is Your Guess? features also highlight women's health issues.

GlycA: A Composite Nuclear Magnetic Resonance Biomarker of Systemic Inflammation
By James D. Otvos, et al.

Nuclear magnetic resonance, or NMR, spectra collected during NMR LipoProfile lipid testing of patient sera contain a signal at 2.00 parts per million of spectral shift the authors of this study have named GlycA. This signal originates from N-acetylglucosamine residues on enzymatically glycosylated acute phase proteins. The authors developed an automated deconvolution procedure to precisely quantify the amplitude of this signal and showed in more than 5,000 participants in the Multi-Ethnic Study of Atherosclerosis that GlycA levels were associated with CRP and other biomarkers of systemic inflammation. Intraindividual variability of GlycA assessed weekly for 5 weeks was low with a CV of 4.3%, comparable to that of cholesterol.

Copy Number Assessment by Competitive PCR with Limiting Deoxynucleotide Triphosphates and High-Resolution Melting
By Luming Zhou, et al.

About 14% of the genome has copy number variations. This article presents a simple method to assess copy number variation by limiting the amount of deoxynucleotide triphosphates (one of the required building blocks for PCR) to maintain relative quantification throughout PCR and into the plateau phase. This method may be used to confirm variants identified by high throughput or genome-wide methods and is rapid and inexpensive.

Importance and Impact of Preanalytical Variables on Alzheimer Disease Biomarker Concentrations in Cerebrospinal Fluid
By Nathalie Le Bastard, et al.

The cerebrospinal fluid biomarker analyses β-amyloid, total tau, and hyperphosphorylated tau are part of the diagnostic criteria of Alzheimer disease. Different preanalytical sample procedures contribute to variability of CSF biomarker levels, hampering between-laboratory comparisons. The aim of this study was to explore the influence of fractionated sampling, centrifugation, freezing temperature, freezing delay, and freeze-thaw cycles on CSF biomarker levels. The authors concluded that temperature of freezing, delay until freezing,

and freeze-thaw cycles significantly influence CSF biomarker concentrations, stressing the need for standard operating procedures for preanalytical sample handling.

Impact of Leading Presenting Symptoms on the Diagnostic Performance of High-Sensitivity Cardiac Troponin T and on Outcomes in Patients with Suspected Acute Coronary Syndrome
By Moritz Biener, et al.

In this study, the authors investigated the role of presenting symptoms including typical chest pain and dyspnea, as well as atypical symptoms on the diagnostic and prognostic accuracy of high-sensitivity cardiac troponin T. Diagnostic accuracy of high-sensitivity cardiac troponin T was higher in patients presenting with typical chest pain as compared to those with dyspnea or atypical symptoms. Dyspnea was associated with the highest risk for death or the combined endpoint of death or AMI after 1 year. Therefore, patients with dyspnea represent a high-risk cohort in which acute coronary syndrome is less frequent than in patients with typical chest pain. The use of higher cutoffs at baseline in addition to the absolute changes in high-sensitivity cardiac troponin T after 6 hours helps to identify non-ST elevation MI in this population

Investigation of 2 Models to Set and Evaluate Quality Targets for Hb A_{1c}: Biological Variation and Sigma-Metrics
By Cas Weykamp, et al.

This paper is about quality targets for Hb A_{1c}. Quality criteria for Hb A_{1c} are becoming important now that Hb A_{1c} is increasingly used for diagnosis. Two models, the biological variation and sigma-metrics model, both based on the concept of Total Analytical Error, have been evaluated for single laboratories and for manufacturer-related groups using data of recent external quality assessment/proficiency testing programs. With a default setting for the quality target and acceptable risk to fail, most individual laboratories and manufacturers pass the criteria of both models. It is concluded that both models are suitable for the intended purpose but that the sigma-metrics model is more flexible.

Continuous Age- and Sex-Adjusted Reference Intervals of Urinary Markers for Cerebral Creatine Deficiency Syndromes: A Novel Approach to the Definition of Reference Intervals
By Lars Mørkrid, et al.

Urinary markers of cerebral creatine deficiency syndromes are known to exhibit large and irregular age variation, and the clinical application of traditional stepwise reference intervals for interpretation of these markers has yielded an unacceptably high rate of false positives. This paper develops a method to derive continuous reference intervals for these markers by data transformation and regression analysis for conversion of covariate-corrected data to z-scores. A broad international collaboration was needed to gather sufficient data for the development of reliable reference intervals. The reference percentiles derived in this study revealed significant gender differences and identified age ranges that were prone to substantial diagnostic misclassification when using current age-

matched reference intervals. The z-scores method described allowed for correction of these gender- and method-specific differences. The authors provide a Web-based algorithm for worldwide use.