Clinical Chemistry

September 2013 Audio Summary

This is the September 2013 issue of *Clinical Chemistry*: Volume 59, Issue 9.

On the cover this month: *A pregnant woman with a flower blossom on her glowing belly.* Pregnancy should be a time of joy and anticipation. Although most pregnancies progress without major complications, one medically important complication is gestational diabetes, a condition associated with adverse outcomes for both the mother and fetus. The prevalence of gestational diabetes is increasing in parallel with the prevalence of obesity and type 2 diabetes. Will more efficient and more scientifically based approaches to diagnosis and treatment keep up with the added demands on healthcare systems? In this issue of *Clinical Chemistry*, Coustan provides readers with an overview of current controversies as well as current recommendations for gestational diabetes care.

The Importance of Commutability of Reference Materials Used as Calibrators: The Example of Ceruloplasmin
By Ingrid Zegers, et al.

This paper describes results from a commutability study performed for reference materials ERM-DA470 and ERM-DA470k/IFCC for ceruloplasmin measurements. The analysis of a large amount of data from the UK NEQAS survey shows that routine methods for ceruloplasmin give discrepant results for fresh patient samples while giving essentially equivalent results for aged patient samples. The results demonstrate how lack of commutability of the reference material can lead to between-method discrepancies. These data provide a well-documented example of the potential consequences of lack of commutability in reference materials and reinforce the importance of commutability of reference materials to the calibration process.

Processed B-Type Natriuretic Peptide Is a Biomarker of Postinterventional Restenosis in Ischemic Heart Disease
By Hirotaka Fujimoto, et al.

Restenosis, a condition in which re-narrowing of the lesion vessel is seen after a coronary intervention procedure, remains a limitation in management. The authors of this study hypothesized that circulating processed forms of B-type natriuretic peptide, might be a biomarker of restenosis. They characterized processed forms of B-type natriuretic peptide by a newly developed mass spectrometry-based immunoassay. Their initial clinical experience suggests that these processed forms are strongly associated with presence of restenosis. Reduced levels of processed forms of B-type natriuretic peptide were seen in patients with restenosis in a cross-sectional study. Measurement of processed forms of B-type natriuretic peptide may serve as a viable potential biomarker to 'rule-out' restenosis.

Fasting Serum Lipid and Dehydroepiandrosterone Sulfate as Important Metabolites for Detecting Isolated Postchallenge Diabetes: Serum Metabolomics via Ultra-High-Performance LC-MS
By Liyan Liu, et al.

A key challenge in patients with isolated post-challenge diabetes is how to make the diagnosis as early as possible using fasting serum which is important for large-scale screening of diabetes. In this study fasting serum metabolomics based on ultra-high-performance liquid chromatography/mass spectrometry was performed to identify biomarkers for the diagnosis of isolated post-challenge diabetes. Linoleic acid, oleic acid, and dehydroepiandrosterone sulfate were associated with greater confidence in the diagnosis of isolated post-challenge diabetes using fasting serum. This study provides useful information to bridge the gaps in understanding regarding the metabolic alterations associated with isolated post-challenge diabetes and might facilitate the diagnosis and characterization of patients with this condition.

Quantitative Insulin Analysis Using Liquid Chromatography–Tandem Mass Spectrometry in a High-Throughput Clinical Laboratory
By Zhaohui Chen, et al.

This article reports a new assay for insulin using mass spectrometry. The authors developed the assay in response to the requirement for a "gold standard" for the measurement of insulin as immunobased techniques can be unreliable. The assay uses the B-chain liberated from the intact molecule as a surrogate for measuring insulin levels in blood. The assay was correlated to a commercial immunoassay and a reference interval was established. The assay is distinguished from previously developed mass spectrometry-based assays in that it is more sensitive and robust, and it has high throughput suitable for a clinical laboratory setting.

Oligosaccharide Analysis in Urine by MALDI-TOF Mass Spectrometry for the Diagnosis of Lysosomal Storage Diseases
By Baoyun Xia, et al.

In this article the authors describe an improved method to generate high resolution oligosaccharide profiles in urine by MALDI-TOF mass spectrometry with greater analytical sensitivity and specificity than current thin layer chromatography methods or the other previously described MALDI-TOF methods. The characteristic oligosaccharide profiles for a broad variety of glycoprotein storage, glycolipid storage as well as glycogen storage conditions are described. The authors also studied possible correlations between the concentrations of the abnormal oligosaccharides and the disease severity in patients, paving the way for using these specific oligosaccharides as potential biomarkers for monitoring disease progression and related treatment.

Cystatin C– and Creatinine-Based Estimates of Renal Function and Their Value for Risk Prediction in Patients with Acute Coronary Syndrome: Results from the PLATelet Inhibition and Patient Outcomes (PLATO) Study
By Axel Åkerblom, et al.

The glomerular filtration rate is an important risk marker for death or myocardial infarction. This study evaluated two commercially available cystatin C assays and their level of agreement in the PLATO trial, a very large acute coronary syndrome population with more than 16000 patients. Despite differences in baseline cystatin C concentrations, overall correlation between the assays was good while the agreement was moderate. The incremental value for risk prediction was very similar for both the two evaluated cystatin C assays, the CKD-EPI equation and for the combined creatinine-cystatin C estimates and no clinical differences were observed.

Reducing Sequence Artifacts in Amplicon-Based Massively Parallel Sequencing of Formalin-Fixed Paraffin-Embedded DNA by Enzymatic Depletion of Uracil-Containing Templates
By Hongdo Do, et al.

Formalin-fixed tissues are used for the detection of mutational biomarkers to determine the treatment of cancer patients. However, sequence errors present major challenges for accurate diagnostics. In this study the authors provide evidence that deamination of cytosines to uracil is the major cause of sequence errors in DNA from formalin-fixed tissues. The authors also provide an effective strategy that allows the majority of those artifacts to be eliminated. This article will of interest to researchers studying cancer mutations and scientists in cancer diagnostics since it provides a simple addition to protocols that will increase the reliability of mutation identification.

Capture of Viable Circulating Tumor Cells in the Liver of Colorectal Cancer Patients
By Eric Denève, et al.

The detection of circulating tumor cells is a rapidly growing segment of cancer research, and the clinical utility of circulating tumor cells as new biomarkers is currently being investigated in more than 250 clinical trials. In this article the authors report that the liver is a major filter organ for EpCAM-positive circulating tumor cells in colorectal cancer, resulting in a predominant decrease in EpCAM-positive circulating tumor cells in the peripheral blood. These results were obtained by the direct comparison of the CellSearch® system, which captures only EpCAM-positive circulating tumor cells, to an independent assay that detected viable EpCAM-positive and EpCAM-negative circulating tumor cells. These findings point to the need of EpCAM-independent circulating tumor cell assays.

Marked Biological Variance in Endocrine and Biochemical Markers in Childhood: Establishment of Pediatric Reference Intervals Using Healthy Community Children from the CALIPER Cohort

By Dana Bailey, et al.

This is a comprehensive study of endocrine and biochemical biomarkers in a large cohort of children and adolescents. The major study objective was to close the critical gaps in pediatric reference values for all endocrine hormones and special chemistry biomarkers, allowing for improved diagnosis and monitoring of children with endocrine and metabolic disorders. The data of this study show marked changes in almost all of the endocrine and biochemical markers studied requiring extensive partitioning of the reference intervals for several of these biomarkers. This database will be of global value when assessing children with endocrine and metabolic disorders.