Clinical Chemistry

March 2014 Audio Summary

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On the cover this month: *Activated platelets*. These irregularly shaped blood components are vital for the normal clotting process. However, platelets also play a role in blood clot formation on arterial stents or on ruptured atherosclerotic plaques, leading to blockage of blood flow and tissue ischemia. For some patients, antiplatelet agents must be used to prevent arterial thrombosis. During therapy, platelet function tests are used to monitor response. Newer approaches to monitoring coagulation, such as viscoelastic coagulation testing, are being introduced. Controversy exists surrounding the tests for monitoring response to antiplatelet therapy or for guiding transfusion decisions in critically ill patients. This issue of *Clinical Chemistry* contains a Q&A in which 4 experts discuss how they define aspirin and clopidogrel response, what platelet function tests are used at their institutions, the role of the laboratory in guiding antiplatelet therapy, and what tests they believe have the greatest potential to predict the risk of bleeding during invasive procedures.

**Invention and Validation of an Automated Camera System That Uses Optical Character Recognition to Identify Patient Name Mislabeled Samples**
By Charles D. Hawker, et al.

This report describes the invention and validation of an automated camera system that uses optical character recognition to identify potentially mislabeled specimens. The authors initiated this project to lower the incidence rate of mislabeled specimens in their laboratory to 0. Among the more than 1 million specimens in the validation study, there were 0 false passes. The optical character recognition system found 121 mislabeled specimens, of which only 71 had been found through the normal quality assurance process. Of the 46 specimens that were further investigated, 21 required issuing corrected reports to the laboratory clients. The authors believe that full implementation of these systems in their laboratory will significantly lower the rate of mislabeled specimens.

**State of the Art for Measurement of Urine Albumin: Comparison of Routine Measurement Procedures to Isotope Dilution Tandem Mass Spectrometry**
By Lorin M. Bachmann, et al.

Urinary albumin is the primary biomarker for detection and monitoring of kidney damage. Harmonized and specific measurement procedures enable use of fixed clinical decision thresholds. To evaluate the current state of harmonization among urine albumin methods, the authors compared the results for 17 routine measurement procedures to an isotope dilution mass spectrometry measurement procedure. An error model approach was used to identify and quantify imprecision and bias components. Bias was found to be the dominant source of error among routine procedures, suggesting that standardization efforts will improve agreement among methods.

**Long-term Prognostic Value for Patients with Chronic Heart Failure of Estimated Glomerular Filtration Rate Calculated with the New CKD-EPI Equations Containing Cystatin C**
By Elisabet Zamora, et al.

The authors of this paper evaluated estimated glomerular filtration rate using the new CKD-EPI equations containing cystatin C and compared the calculated values with those obtained by the MDRD-4-IDMS and the CKD-EPI equations.
The results indicated that the CKD-EPI equations containing cystatin C were useful for heart failure risk stratification and had better performance measurements than the other two equations. Notably, the two new CKD-EPI equations containing cystatin C showed the best reclassification performance as compared with the creatinine-only based estimated glomerular filtration rate equations MDRD-4-IDMS and CKD-EPI in those patients with estimated glomerular filtration rate between 45-74.9 mL per minute per 1.73 square meter. These new equations appear to be useful for assessing prognosis of heart failure patients with moderate renal insufficiency.

**Genetic Variation in KLK2 and KLK3 Is Associated with Concentrations of hK2 and PSA in Serum and Seminal Plasma in Young Men**
By Charlotta Sävblom, et al.

Genetic variation near the genes coding for prostate-specific antigen and human kallikrein-related peptidase 2 have been associated with serum concentrations of these proteins and prostate cancer risk in older men. The authors of this paper asked whether these SNPs are associated with secreted levels of these proteins in young men without prostate disease by testing for association between SNPs at these genes with protein concentrations in serum and seminal plasma. They found several SNPs associated with concentrations of these proteins in both the serum and seminal plasma. These data suggest that genetic variation may be useful in refining models of PSA cut-off values in prostate cancer testing.

**Rapid Electrokinetic Isolation of Cancer-Related Circulating Cell-Free DNA Directly from Blood**
By Avery Sonnenberg, et al.

Conventional methods to isolate circulating cell-free DNA from blood are time-consuming, laborious, and expensive. The authors of this study used an AC electrokinetic device to isolate circulating cell-free DNA from 25 microliters of unprocessed blood from 15 chronic lymphocytic leukemia patients and 3 normal individuals. The isolation process required less than 10 minutes. Results obtained by this method matched results obtained using conventional methods requiring much more time and larger samples. Rapid isolation of circulating cell-free DNA directly from a drop of blood will advance disease-related biomarker research, accelerate the transition from tissue to liquid biopsies, and enable point-of-care diagnostic systems for patient monitoring.

**Performance of Direct Estradiol Immunoassays with Human Male Serum Samples**
By David J. Handelsman, et al.

In this report the authors studied the accuracy of 5 widely used commercial estradiol immunoassays as compared with the reference method of liquid chromatography mass spectrometry. This analysis used a reference set of 101 serum samples from healthy older men. The authors found that none of the 5 immunoassays had good accuracy. These results reinforce a growing awareness of the need to switch to the use of more reliable mass-spectrometry-based estradiol assays.

**Pediatric Within-Day Biological Variation and Quality Specifications for 38 Biochemical Markers in the CALIPER Cohort**
By Dana Bailey, et al.

Studies of biological variation provide insight into the physiological changes that occur within and between individuals. Values obtained from such investigations are crucial for patient monitoring and for establishing quality specifications. To date, few investigations have explored biological variation in a pediatric population. This study evaluated the short-term biological variation of 38 analytes in a pediatric population and compared findings to adult values. Although the short-term biological variation results for approximately 70% of analytes in the pediatric population were consistent with those for adults, 11 analytes showed differences between the adult and pediatric population. These data highlight the need for further studies of biological variation in the pediatric population.

**Increased Soluble ST2 Predicts Long-term Mortality in Patients with Stable Coronary Artery Disease: Results from the Ludwigshafen Risk and Cardiovascular Health Study**
By Benjamin Dieplinger, et al.

Soluble ST2 has emerged as a clinically useful prognostic biomarker in patients with heart failure and myocardial infarction. The aim of this study was to evaluate the long-term (median follow-up of 9.8 years) prognostic value of soluble ST2 in 1,345 patients with stable coronary artery disease undergoing coronary angiography. In this well-established cohort of patients with stable coronary artery disease, soluble ST2 was an independent predictor for long-term all-cause and cardiovascular mortality and added prognostic value to the routinely used cardiac biomarkers NT-pro B-type natriuretic peptide and high-sensitivity cardiac troponin T. Thus, a combination of these 3 complementary biomarkers may provide a promising tool for outcome prediction in patients with stable coronary artery disease.

**Interlaboratory Agreement of Insulin-like Growth Factor 1 Concentrations Measured by Mass Spectrometry**
By Holly D. Cox, et al.

In this article the authors determined the interlaboratory agreement of endogenous protein measurements by liquid chromatography-tandem mass spectrometry. They focused on insulin-like growth factor-1, a biomarker used in the diagnosis of certain growth disorders and in the detection of doping with growth hormone in sports. The results demonstrate that mass spectrometric measurements of proteins can be very reproducible between laboratories. In addition, a single-point native human serum calibrator can reduce bias between laboratories. This study provides additional strong support for moving forward the clinical measurement of proteins by mass spectrometry in clinical laboratories.

**B-Type Natriuretic Peptide Forms within the Heart, Coronary Sinus, and Peripheral Circulation in Humans: Evidence for Degradation before Secretion**
By Patalee G. Mahagamasekera, et al.

Circulating B-type natriuretic peptide, secreted by the heart, contributes to circulatory homeostasis, but its molecular forms remain undefined. This study assessed B-type natriuretic peptide forms in cardiac tissue and peripheral plasma at cardiac transplantation and in coronary sinus and peripheral plasma during cardiac catheterization. B-type natriuretic peptide was found to be degraded substantially within cardiac tissues in individuals with terminal heart failure, and only metabolites of B-type natriuretic peptide were found to be present in coronary sinus and peripheral plasma in patients with preserved systolic function. The demonstrated degradation of B-type natriuretic peptide to metabolites of presumed low bioactivity before entry into the circulation suggests that blockade of degrading enzymes, yet to be defined, may lead to improved treatment for heart failure.