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On the cover this month: Disruptive Innovation. Disruptive innovations are innovations that have created new markets for new categories of customers. In laboratory diagnostics, disruptive innovations will likely make the greatest impact during the next 25 years by lowering costs without compromising quality and performance, ultimately lowering the costs of health care overall. Additionally, innovations that improve existing technologies (e.g., PCR, point-of-care devices, mass spectrometry) may hold answers for some of the most challenging diagnostic problems of today. This month we highlight 2 features that draw attention to the importance of disruptive innovations. The first is an opinion piece, published in this issue of *Clinical Chemistry*, on why disruptive innovations matter in laboratory diagnostics. The second is a Tuesday afternoon symposium at the 2015 AACC Annual Meeting in Atlanta, entitled "*Clinical Chemistry*'s Hot Topics of 2015: Disruptive Innovation in Laboratory Medicine," in which 3 examples of disruptive innovation, some of which have been published in *Clinical Chemistry*, will be discussed and their impacts highlighted.

Recalibration of Blood Analytes over 25 Years in the Atherosclerosis Risk in Communities Study: Impact of Recalibration on Chronic Kidney Disease Prevalence and Incidence
By Christina M. Parrinello, et al.

This study assessed the comparability of 8 biomarker measurements over 25 years in the Atherosclerosis Risk in Communities Study. For analytes lacking comparability, calibration corrections were determined. Trends in analyte concentrations were assessed before and after calibration. Analytes were re-measured in stored samples from 200 participants. Original values were calibrated to re-measured values using Deming regression. Repeat measures were highly correlated with the original values, but creatinine and uric acid had differences greater than 10%, and correction equations were applied to the entire cohort. Chronic kidney disease prevalence differed substantially after calibration of creatinine. These data demonstrate the importance of calibration of laboratory assays, and the authors encourage such calibration studies in large epidemiologic cohorts.

Application of the Characteristic Function to Evaluate and Compare Analytical Variability in an External Quality Assessment Scheme for Serum Ethanol
By Wim Coucke, et al.

In this study the authors applied the characteristic function in the clinical laboratory field using data from an External Quality Assessment Scheme of serum ethanol. The function was extended to offer statistical inference about method comparisons. The study provides a detailed overview of the application of the function, how to extend it, and how to interpret the results. Results showed that the increase in the standard deviation with increasing target concentration was slower for Abbott and Roche than for other methods. The characteristic function may offer new insights to evaluate analytical method variability.

Tandem Mass Spectrometric Determination of Atypical 3β-Hydroxy-Δ^5-Bile Acids in Patients with 3β-HydroxyΔ^5-C_{27}-Steroid Oxidoreductase Deficiency: Application to Diagnosis and Monitoring of Bile Acid Therapeutic Response
By Wujuan Zhang, et al.

In this article the authors present a tandem mass spectrometry method for the measurement of 3β-hydroxy-Δ^5-bile acid sulfates in urine that is applicable to the diagnosis and accurate monitoring of responses to primary bile acid therapy in patients with 3β-hydroxyΔ^5-C_{27}-steroid oxidoreductase deficiency, a progressive cholestatic liver disease. Evidence is presented that conventional GC-MS is not a reliable method for measuring these bile acid sulfates, which are labile and acid sensitive. The authors also report the typical urinary concentrations of these hepatotoxic bile acids found in the patients with 3β-hydroxyΔ^5-C_{27}-steroid oxidoreductase deficiency at the time of diagnosis and following primary bile acid therapy.

Age- and Sex-Specific Dynamics in 22 Hematologic and Biochemical Analytes from Birth to Adolescence
By Jakob Zierk, et al.

Results of laboratory tests in children and adolescents have to be interpreted in the context of age- and sex-dependent dynamics. Reference intervals for separate age groups, however, can only approximate these dynamics. Ethical and practical constraints restrict blood sampling from healthy community children for the creation of continuous reference intervals. This study employed an indirect method to generate continuous reference intervals for 22 hematological and biochemical analytes by analyzing a clinical laboratory database. The provided reference intervals capture the changes in laboratory analytes during pediatric development more accurately than use of separate age groups and allow a more precise consideration of these dynamics in clinical decision making.

Noninvasive Detection of Activating Estrogen Receptor 1 (*ESR1*) Mutations in Estrogen Receptor–Positive Metastatic Breast Cancer
By David S. Guttery, et al.

Activating mutations of the estrogen receptor gene can drive resistance to endocrine therapies. Using next generation sequencing and digital droplet PCR, the authors detected activating mutations in estrogen receptor 1 in 18.8% of 48 cell free DNA samples from estrogen receptor positive metastatic breast cancer patients and in one primary patient who was disease free by imaging. The authors also demonstrate the emergence of multiple mutations in cell free DNA on therapy. Lastly, the authors detected overlapping mutation profiles in cell free DNA and circulating tumor cells. The results from this study suggest that detecting activating estrogen receptor 1 mutations in cell free DNA and circulating tumor cells could allow for cessation of ineffective endocrine therapies and switching to other treatments prior to the emergence of metastatic disease.

High-Sensitivity Cardiac Troponin T Concentrations below the Limit of Detection to Exclude Acute Myocardial Infarction: A Prospective Evaluation

By Richard Body, et al.

In previous work, patients with initial high-sensitivity troponin concentrations below the limit of blank in the Emergency Department had an extremely low probability of acute myocardial infarction. This low probability of myocardial infarction could reduce the need for serial sampling. In this study of 463 patients, no patients with a troponin below 3 nanograms per liter, the assay limit of blank, had an acute myocardial infarction, although this represented only 5.2% of patients. However, acute myocardial infarction could have been excluded in all of the 17.3% of patients with no electrocardiographic signs of ischemia and troponin below 5 nanograms per liter, the assay limit of detection. These findings support the safety of this approach in practice for ruling out acute myocardial infarction.