Clinical Chemistry

September 2016 Audio Summary

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ON THE COVER: A mother holding a 4-month-old baby born with microcephaly. First discovered in primates in the Zika Forest of Uganda in 1947, the once obscure Zika virus, now known to cause birth defects such as microcephaly, has been declared an international health emergency by the World Health Organization. This issue of *Clinical Chemistry* contains a timely Q&A article in which three experts currently involved in the response to Zika share their knowledge and their insights on what we have learned to date, even as the epidemic continues to unfold.

Alcohol consumption and cardiac biomarkers: The Atherosclerosis Risk in Communities (ARIC) Study
By Mariana Lazo, et al.

Moderate alcohol consumption has been associated with reduced risk of cardiovascular disease, however the mechanisms remain unclear. High sensitivity cardiac troponin T and NT proBNP are two novel biomarkers of cardiac damage and stress, respectively, and may help improve our understanding of the full cardiovascular effects of alcohol consumption. This study characterized the cross-sectional and prospective association of alcohol consumption with subclinical myocardial damage and stress, as assessed by high sensitivity cardiac troponin T and NT-proBNP in a large community-based population of adults without existing cardiovascular disease. The results indicated that moderate drinking was associated with decreased odds of increases in high sensitivity cardiac troponin T; in contrast there was a positive association between current alcohol consumption and NT-proBNP concentrations and with incident increases in NT-proBNP. These study results highlight the complexity of the association between alcohol consumption and cardiovascular disease that hinder a universal recommendation on alcohol consumption.

Modification and Validation of the Triglyceride-to–HDL Cholesterol Ratio as a Surrogate of Insulin Sensitivity in White Juveniles and Adults without Diabetes Mellitus: The Single Point Insulin Sensitivity Estimator (SPISE)
By Katharina Paulmichl, et al.

The triglyceride-to-HDL-cholesterol-ratio was introduced as a promising tool to estimate insulin resistance. Easier and more affordable tools to estimate insulin resistance are of interest for both pediatric and adult patient care. In this study the study population included adults as well as adolescents. Participants underwent oral-glucose-tolerance-tests and euglycemic clamp-tests. To refine the triglyceride-to-HDL-cholesterol -ratio, mathematical modeling was applied including body mass index, triglyceride and HDL cholesterol and compared to traditional insulin sensitivity indices. A newly derived index called the Single Point Insulin Sensitivity Estimator (SPISE) index seemed well suited as a surrogate for whole-body insulin-sensitivity. The index is derived from inexpensive fasting laboratory test measurements from a single-point blood draw and anthropometric measurements in adolescents and adults.

Serum Cortisol: An Up-To-Date Assessment of Routine Assay Performance
By James M Hawley, et al.

Serum cortisol proficiency testing schemes regularly demonstrate a wide dispersion of results. The authors of this study used a total serum cortisol candidate reference measurement procedure to provide an up-to-date assessment of the performance characteristics of 6 routine cortisol assays. They established cohorts of normal males, normal females, pregnant patients and patients prescribed either prednisolone or metyrapone, to investigate the effects of gender, matrix, and antibody specificity on cortisol quantification. Their results demonstrated that the accuracy of immunoassay cortisol quantification is compromised by both matrix effects and antibody non-specificity. This work highlights a deficiency in the standardization of routine cortisol assays.

Real-Time Quantification of Amino Acids in the Exhalome by Secondary Electrospray Ionization–Mass Spectrometry: A Proof-of-Principle Study
By Diego García-Gómez, et al.

Amino acids are frequently determined in clinical chemistry. However, current analysis methods are time-consuming, invasive, and suffer from artifacts during sampling, sample handling, and sample preparation. The authors of this study describe a novel breath analysis technique that detects amino acids directly and non-invasively in exhaled breath in real-time. The levels in breath were found to correlate with plasma concentrations. This approach should facilitate efficient diagnostics and give insights into human physiology.

Multiplex Droplet Digital PCR Quantification of Recurrent Somatic Mutations in Diffuse Large B-Cell and Follicular Lymphoma
By Miguel Alcaide, et al.

The clinical and research community needs accurate and sensitive assays to inform on the diagnosis, response and disease progression of cancer malignancies. This work demonstrates the enormous benefits of droplet digital PCR for either the invasive or non-invasive genetic profiling of solid tumors. New assays for detecting recurrent mutations in patients with some common forms of non-Hodgkin lymphoma are presented, along with more general principles for designing such assays for other tumor types. The work includes examples of the utility of these assays when applied to patient samples and introduces novel applications such as uniplex and inverted droplet digital PCR assays.

Simultaneous Testing for 6 Lysosomal Storage Disorders and X-Adrenoleukodystrophy in Dried Blood Spots by Tandem Mass Spectrometry
By Silvia Tortorelli, et al.

Newborn screening for lysosomal storage disorders has revealed that late onset variants of these conditions are unexpectedly frequent. The authors of this study developed an efficient and cost-effective multiplex assay using tandem mass spectrometry to diagnose six lysosomal storage disorders and several peroxisomal disorders in patients presenting with diverse phenotypes at any age. They combined previously described methods to measure simultaneously activities of six lysosomal enzymes and lysophosphatidylcholines in dried blood spots by flow injection tandem mass spectrometry. The assay performed with a sensitivity of 100% and specificity of 95.7%. The positive predictive value and false positive rate were 51% and 4% respectively. The assay allows for a rapid and effective screening assay for Hurler disease, Gaucher disease, Niemann-Pick A/B disease, Pompe disease, Krabbe disease, Fabry disease, X-adrenoleukodystrophy, and peroxisomal biogenesis disorder in dried blood spots using FIA-tandem mass spectrometry that is amenable to high-throughput population screening.

Analytical Bias Exceeding Desirable Quality Goal in 4 out of 5 Common Immunoassays: Results of a Native Single Serum Sample External Quality Assessment Program for Cobalamin, Folate, Ferritin, Thyroid-Stimulating Hormone, and Free T4 Analyses
By Gunn BB Kristensen, et al.

This study used single serum samples to evaluate method differences for five immunoassays (cobalamin, folate, ferritin, free T4 and TSH). Further the authors explored whether the use of method dependent reference intervals may compensate for method differences and investigated commutability of commercial EQA materials. The results showed a bias between the measurement procedures that was unacceptably large for 4/5 of the tested components. Traceability to reference materials as claimed by the diagnostic industry did not lead to acceptable harmonization. Adjustment of reference intervals in accordance with method differences and use of commutable external quality assessment samples were commonly not implemented.

How Well Do Laboratories Adhere to Recommended Clinical Guidelines for the Management of Myocardial Infarction: The CARdiac MArker Guidelines Uptake in Europe Study (CARMAGUE)
By Paul O. Collinson, et al.

This study assessed the current use of evidence-based guidelines for the use of cardiac biomarkers in Europe and North America. In 2013/14 a web-based questionnaire was distributed via North American and European biochemical societies. Questions included cardiac biomarkers measured and decision thresholds. In Europe returns were obtained from 442 hospitals, and in North America there were 91 responses. Cardiac troponin was the preferred cardiac biomarker and first line marker. There were substantial differences in the choice of decision limits and their derivations. This probably relates to different availability of assays between Europe and North America and different laboratory practices on assay introduction.