Clinical Chemistry

February 2016 Audio Summary

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ON THE COVER Colored transmission electron micrograph of a Clostridium difficile bacterium forming an endospore. This Grampositive anaerobic bacillus, normally present in small numbers in the gut, can proliferate when intestinal resistance is low, producing a toxin that causes diarrhea and more serious conditions such as pseudomembranous colitis. Antibiotics can be used to treat pseudomembranous colitis, but the highly resistant spores formed by the bacteria often cause elapses. This is just one reason why antibiotic resistant C. difficile is considered one of the most urgent threats to public health. This issue of *Clinical Chemistry* contains a Q&A in which 4 experts with different roles in this field were asked to share their thoughts on contemporary challenges in diagnosing, treating, and preventing C. difficile infection.

Increased Baseline C-Reactive Protein Concentrations Are Associated with Increased Risk of Infections: Results from 2 Large Danish Population Cohorts
By Jeppe Zacho et al.

The acute phase-reactant C-reactive protein increases rapidly during an infection. Chronic low-level increases in C-reactive protein could be associated with an increased risk of infectious disease. The authors of this report studied 70,000 persons from two general population studies. In the combined populations, individuals in the highest C-reactive protein tertile compared to the lowest, had a 1.7 fold increased risk of bacterial diseases, but no detectable increase in the rates for viral, mycosis, and parasitic diseases. The increased risk was mainly carried by pneumonia, sepsis, and particularly Gram negative infections. None of the genotype combinations based on four CRP polymorphisms were associated with an increased risk of infectious disease.

Identification of Males with Cryptic Fragile X Alleles by Methylation-Specific Quantitative Melt Analysis
By Solange M Aliaga et al.

Fragile X Syndrome is a common, genetic cause of intellectual disability and autism. It is usually caused by an abnormal DNA sequence expansion in the FMR1 gene, called a full mutation. The authors of this study found ten undetected mosaics in more than 3000 referrals who had normal size FMR1 sequence and a full mutation when tested using the currently recommended method. They identified these individuals using a new test called Methylation-Specific Quantitative Melt Analysis. Most showed cognitive impairment and/or autism even at low levels of mosaicism for full mutation alleles.

Analytical Performance of Multiplexed Screening Test for 10 Antibiotic Resistance Genes from Perianal Swab Samples
By George Terrance Walker et al.

This paper describes a novel molecular diagnostic test for detection of ten antibiotic resistance gene families from perianal swabs. The test is designed to screen patients for colonization or infection with multi-drug resistant bacteria. The test uses a novel microfluidic format with excellent sensitivity and high sample throughput.

Short- and Long-term Biologic Variability of Galectin-3 and Other Cardiac Biomarkers in Patients with Stable Heart Failure and Healthy Adults.
By Emily I Schindler et al.

This study examines the within individual biologic variability of the cardiac biomarker Galectin-3. Galectin-3 has been proposed to have predictive value in patients with heart failure. The authors examined 3 week and 3 month within individual variability in 20 healthy individuals and 39 patients with stable heart failure. Within individual variability of Galectin-3 expressed as coefficient of variation was less than 10% for short- and long-term periods in both populations. This low amount of biologic variability makes Galectin-3 even more promising as a potentially useful biomarker for heart failure patients.

Effect of Blood Collection Time on Measured Δ9-Tetrahydrocannabinol Concentrations: Implications for Driving Interpretation and Drug Policy
By Rebecca Lynn Hartman et al.

In "driving under the influence" cases, blood typically is collected 1.5 to 4 hours after an incident. Here the authors evaluated how rapidly-decreasing blood tetrahydrocannabinol, or THC concentrations, could complicate toxicological interpretation. Participants inhaled vaporized cannabis and then drove a simulator from 0.5 to 1.3 hours post-dose. Blood THC concentrations were determined up to 8.3 hours. Eighteen participants' median concentration decreased by more than 90%, with a range of 53.8 to 100%, from the maximal concentration by 1.4 hours post-dose. With residual THC, concentrations rapidly decreased to pre-inhalation baselines. During-drive concentrations previously associated with impairment, that is, greater than 8.2μg/L, decreased to a median of less than 5μg/L by 3.3 hours post-dose and less than 2μg/L by 4.8 hours; only one participant had THC greater than 5μg/L after 3.3 hours. The results show that forensic blood THC may be lower than common cutoffs despite exceeding these cutoffs while driving.

Potential involvement of Jagged1 in metastatic progression of human breast carcinomas
By Natalia Bednarz-Knoll et al.

The current study shows that Jagged1 expression is found in 50% of tumors from breast cancer patients and also in 86% of the circulating tumor cells from metastatic breast cancer patients, indicating aggressive characteristics of a tumor and poor patients' outcome. This is the first report showing that Jagged1 expression might support tumor dissemination and resistance to bisphosphonates-based therapy. These results imply that Jagged1 might play a role in breast cancer progression and has a potential to serve as a biomarker and target to modulate resistance to bisphosphonates-based therapy.

Impact of Implementing Preanalytical Laboratory Standards on the Diagnosis of Gestational Diabetes Mellitus: A Prospective Observational Study
By Niamh Daly et al.

Women being screened selectively for gestational diabetes mellitus at 24-32 weeks were recruited at their convenience before their 75-g Oral Glucose Tolerance Test. The authors of this study evaluated glucose concentrations and

the incidence of gestational diabetes mellitus after implementation of the American Diabetes Association preanalytical guidelines, compared with usual hospital conditions. Paired samples were taken. One sample followed American Diabetes Association recommendations and was transferred to the laboratory on an iced slurry for immediate separation and analysis. The second sample was handled in the usual hospital conditions. Implementation of the American Diabetes Association preanalytical glucose sample handling recommendations resulted in higher glucose concentrations, and in a 2.7-fold increase in detection of gestational diabetes mellitus as compared with non-implementation.

Multianalyte Conventional Reference Material (MacRM): A Useful Tool for Nationwide Standardization of Laboratory Measurements for Medical Care—A Model Study in Japan
By Katsuyuki Shinohara et al.

The Japanese Committee for Clinical Laboratory Standards has developed a multianalyte conventional reference material for nationwide standardization of laboratory measurements. Pooled sera were obtained from healthy Japanese people. Target values of the pooled sera for 30 analytes were assigned based on the measurement results of 45 reference laboratories whose calibration was verified by measuring nationally certified reference materials. Survey specimens were prepared by essentially the same method used for the reference material preparation but without assigning target values. Commutability of the reference material was confirmed for 30 analytes with sera from 150 individual patients. The multianalyte reference material was successfully applied as a calibrator to achieve nationwide standardization for 30 analytes measured by 165 laboratories that used various methods from different manufacturers.