Clinical Chemistry

April 2014 Audio Summary

This is the April 2014 issue of *Clinical Chemistry*, Volume 60, Issue 4.

On the cover this month: *Fred Apple.* When you think of Dr. Fred Apple, the term troponin immediately comes to mind. An internationally recognized clinical chemist who has traveled the world, Fred has never wandered from Minneapolis, where he took his first job teaching physics (yes, physics) in the local school district. If associating Dr. Apple with physics, rather than clinical chemistry, is hard to imagine, how about the fact that he owes his very existence to hay fever? And how about his link to Robert Frost, Woodstock, the Grateful Dead, and the 1970 March on Washington? If you want to know about the two sides of a truly gold coin, read about Dr. Apple in this issue's Inspiring Minds.

Magnetically Promoted Rapid Immunoreactions Using Functionalized Fluorescent Magnetic Beads: A Proof of Principle
By Satoshi Sakamoto, et al.

Accurate and rapid detection of biomarkers is essential to understanding disease states. However, lack of reliable protocols often limits efficient medical diagnosis. In this study the authors aimed at constructing rapid biomarker detection systems with functional materials, and then developed a rapid immunoreaction system using polymer-coated fluorescent ferrite beads. By magnetic collection of antibody-coated fluorescent ferrite beads to a specific place followed by direct fluorescence measurement, a high-speed sandwich immunoassay or immunohistochemical staining could be achieved. Immunoreactions involving the magnetic collection of antibody-coated fluorescent ferrite beads allowed not only dramatic acceleration of the antigen-antibody reaction but also improvement of analytical sensitivity.

Sandwich Assay for Tacrolimus Using 2 Antitacrolimus Antibodies
By Tie Q. Wei, et al.

The authors of this study developed a sandwich assay for a hapten drug FK506. The authors conducted an epitope analysis utilizing the binding properties of drug analogs or metabolites to conclude that separate epitopes existed for 2 anti-FK506 antibodies. A sandwich assay was formulated and confirmed based on this analysis. Sandwich assays for small haptens lower metabolite cross-reactivity and provide more specific drug measurements than the conventional competitive immunoassays.

Phase I and II Cannabinoid Disposition in Blood and Plasma of Occasional and Frequent Smokers Following Controlled Smoked Cannabis
By Nathalie A. Desrosiers, et al.

Cannabis is the most commonly abused illicit drug. The differences between frequent and occasional cannabis smokers need further characterization, especially for phase II metabolites. The authors of this study recruited 14 frequent and 11 occasional smokers to comprehensively document the disposition of 7 cannabinoids in human blood and plasma for 30 hours following ad libitum smoking of a 6.8% Δ^9-tetrahydrocannabinol cigarette. Significantly higher Δ^9-tetrahydrocannabinol and metabolite concentrations were documented in frequent

smokers owing to the high cannabinoid body burden developed with frequent smoking. For blood Δ^9-tetrahydrocannabinol greater than 5 µg/L, 2 frequent smokers were still positive at 30 hours and 2 occasional smokers were never positive.

Effects of Measurement Frequency on Analytical Quality Required for Glucose Measurements in Intensive Care Units: Assessments by Simulation Models
By James C. Boyd and David E. Bruns

Total-error allowances have been proposed for glucose meters used in tight-glucose-control protocols. It is unclear whether these proposed quality specifications are appropriate for continuous glucose monitoring. The authors of this study performed Monte Carlo simulations of patients on tight-glucose-control protocols. To simulate use of glucose meters, measurements were made hourly. To simulate continuous glucose monitoring, glucose measurements were made every 5 minutes. The adverse effects of measurement imprecision on the rates of hypoglycemia and hyperglycemia and glycemic variability were found to be lower at the higher measurement frequency. Current quality specifications for imprecision of glucose meters do not appear to be transferable to continuous glucose monitoring.

Publication and Reporting of Test Accuracy Studies Registered in ClinicalTrials.gov
By Daniel A. Korevaar, et al.

Nonpublication and selective reporting have been demonstrated several times in the biomedical literature. This study investigated, for the first time, their extent in the field of medical testing. The study found that in a cohort of diagnostic and prognostic test accuracy studies registered in ClinicalTrials.gov, only 45% were published within 30 months after their completion. Discrepancies between registered records and corresponding publications were frequent, especially regarding the outcomes. Although the International Committee of Medical Journal Editors does not require registration of test accuracy studies, these results indicate that prospective registration is also important in this research field and should be further promoted.

Isothermal Recombinase Polymerase Amplification Assay Applied to the Detection of Group B Streptococci in Vaginal/Anal Samples
By Rana K. Daher, et al.

This paper focused on evaluating the performance of the isothermal recombinase polymerase amplification technique in the rapid and sensitive screening of pathogens. The authors compared the clinical performance of isothermal recombinase polymerase amplification to rtPCR for the detection of Streptococcus agalactiae in vaginal or anal samples from 50 pregnant women. Their findings showed similar performance of isothermal recombinase polymerase amplification to rtPCR in terms of clinical sensitivity and specificity. However, isothermal recombinase polymerase amplification surpassed rtPCR in time-to-result reducing it to less than 20 min. Isothermal recombinase polymerase amplification appears

to be potentially useful at point-of-care as a molecular diagnostic tool, and its implementation into microsystems may obviate the need for sophisticated instrumentation.

Screening Method to Evaluate Point-of-Care Human Chorionic Gonadotropin (hCG) Devices for Susceptibility to the Hook Effect by hCG β Core Fragment: Evaluation of 11 Devices
Robert Nerenz, Haowei Song, and Ann M. Gronowski

hCG β core fragment can cause false negative results in point-of-care hCG devices. The authors of this study describe a screening method to evaluate point-of-care hCG devices for the this effect and evaluate the performance of 11 devices. Only 2 devices exhibited minimal to no susceptibility to hCG β core fragment. Devices that gave the strongest signal with hCG β core fragment alone were least affected by the false negative effect. The screening method described here can be used by device users and manufacturers to evaluate point-of-care devices for susceptibility to inhibition by hCG β core fragment.

Posttransplantation Bone Marrow Assessment by Quantifying Hematopoietic Cell–Derived mRNAs in Plasma Exosomes/Microvesicles
By Jun Aoki, et al.

Bone marrow aspiration is a painful medical procedure, but cannot be avoided when assessments of hematopoietic precursor cells are needed, because these cells exist only in bone marrow and rarely escape to peripheral blood. The authors of this study isolated exosomes and microvesicles from peripheral blood plasma and successfully quantified bone marrow-derived myeloid-, erythroid-, and megakaryocyte-lineage-specific polyadenylated mRNAs in 18 patients undergoing hematopoietic stem cell transplantation. Blood levels of mRNAs gave a much earlier indication of bone marrow recovery than conventional complete blood count and were predictive of the final clinical outcome. Thus, plasma mRNAs carried in exosomes and microvesicles may represent new biomarkers for the assessment of bone marrow condition.

Quantification of Tau in Cerebrospinal Fluid by Immunoaffinity Enrichment and Tandem Mass Spectrometry
By Thomas McAvoy, et al.

Cerebrospinal fluid Tau is a common biomarker for Alzheimer disease typically measured using sensitive immunoassays. Given the molecular diversity of Tau in cerebrospinal fluid, the selectivity of these immunoassays has often been questioned. To address these concerns, the authors of this study developed a sensitive and highly specific mass spectrometry-based assay to measure Tau by combining immunoaffinity enrichment with microflow liquid chromatography tandem mass spectrometry. This first-of-its-kind assay represents an important tool to better characterize or standardize cerebrospinal fluid Tau immunoassays and can potentially be used to measure other posttranslationally modified forms of Tau in cerebrospinal fluid.