

This is the May 2016 issue of Clinical Chemistry, Volume 62, Issue 5.

ON THE COVER *W. Greg Miller*. If science had not intervened in his life, we might have known him as Father Miller instead of Doctor Miller. Fortunately for us, he ended up in clinical chemistry. He is an avid sport and racecar driver and enthusiast, an avocation where apparently some praying has been in order while Greg has been at the wheel. He approaches his hobby the same way he approaches his work life — with precision and fast pace — having succeeded at both. This month's *Inspiring Minds* article explores the many facets of Greg Miller, a personal story that is indeed "inspiring."

The importance of reagent lot registration in external quality assurance/proficiency testing schemes

By Anne Stavelin, et al.

Providers of external quality assurance schemes have traditionally had little focus on reagent lot variation. The present paper shows the importance of lot-to-lot variation detected in the Noklus schemes for urine albumin/creatinine ratio and international normalized ratio. The lot differences found in the albumin/creatinine ratio scheme were valid also for patient samples whereas this was not the case for the international normalized ratio scheme. The reagent lot results are important for how the feedback reports are interpreted and may explain deviant results. Providers of external quality assurance schemes are encouraged to register and evaluate results from reagent lots.

Postmarket Surveillance of Point-of-Care Glucose Meters through Analysis of Electronic Medical Records

By Lee F Schroeder, et al.

FDA approval and laboratory validation of point-of-care glucose meters are limited in scope and size. As a result, meter performance over time, and in heterogeneous populations, is relatively unknown. The authors of this study demonstrate that analyzing coincident testing events, defined as near-in-time point-of-care and central laboratory glucose testing in the same patient, enables ongoing postmarket surveillance. They demonstrate equivalence between analyzing coincident testing and a prospective bedside ICU study, as well as near equivalence to a laboratory validation study. Given the large number of data points used, their method enables rigorous analysis of interferences due to pharmaceuticals or extremes of physiology.

Biological variation: The effect of different distributions on the estimated within-subject variation and reference change values

By Thomas Røraas, et al.

Good estimates of the within-subject biological variation are essential both for diagnosing and monitoring patients and for setting analytical performance specifications. This study performed computer simulation modeling of biological variation data assuming various data distributions. Based on the simulated data the performance of three different methods for estimating biological variation and calculating the reference change value were evaluated. Clear performance differences were seen between methods for estimating biological variation and reference change values. The authors recommend against use of the usual methods for calculating within-subject biological variation and reference change values.

Early Phase Studies of Biomarkers: What Target Sensitivity and Specificity Values Might Confer Clinical Utility?

By Margaret S Pepe, et al.

Discovery and early validation research of biomarkers requires specifying target levels for biomarker accuracy, *vis-à-vis* sensitivity and specificity for the clinical outcome, that could lead to a useful clinical test. If a biomarker reaches those target levels of accuracy, further development and study of the marker may be warranted. Unfortunately, methods for calculating target accuracy are not currently available. The authors of this paper describe an approach for calculating target levels of biomarker sensitivity and specificity. They apply the method for biomarker research in three contexts: predicting colon cancer recurrence; predicting interval breast cancers after mammographic screening; and screening for ovarian cancer.

Optimization and Standardization of Circulating microRNA Detection for Clinical Application: the "miR-Test" case

By Matteo J Marzi, et al.

The clinical transferability of diagnostic tests based on the detection of circulating microRNAs is still uncertain due to insufficient standardization and optimization in the clinical setting. This report describes the results of the extensive analyses that have been performed on a signature that is based on the expression of circulating microRNAs for lung cancer detection, to optimize the sensitivity and reproducibility of microRNA quantification from clinical serum samples, while minimizing experimental variability at the analytical and pre-analytical levels. The authors propose their methodology as a key reference for the development of clinical-grade tests based on circulating microRNAs.

The Prospective Associations of Systemic and Urinary Choline Metabolites with Incident Type 2 Diabetes

By Gard FT Svingen, et al

Patients with type 2 diabetes show signs of altered choline metabolism; however prospective associations between choline related metabolites and risk of incident type 2 diabetes have been explored only to a limited degree. This study examined such relationships among over 3000 non-diabetic patients from Norway, who were followed up for over seven years. Lower plasma betaine, as well as higher urine dimethylglycine, betaine and sarcosine, were found to be strongly related to incident type 2 diabetes, also when adjusted for potential confounders and traditional risk markers. These results suggest that altered choline metabolism may be a feature of patients at risk of developing type 2 diabetes.

Diagnosis and monitoring of cystinosis using immunomagnetically purified granulocytes

By Ilya Gertsman, et al.

Leukocyte cystine measurement has been the key measurement to diagnose and monitor cystinosis, but with existing methodology, reliable results can only be obtained when samples are prepared at the point of care; this restriction limits access to testing for patients who do not live near medical centers that can carry out the sample processing. The new assay validated in this manuscript permits samples of whole blood to be sent, and its use of granulocytes, a much more homogeneous tissue, should give more consistent results. This assay represents a significant advance to the care of patients with cystinosis.

The New Substance Abuse and Mental Health Services Administration Oral Fluid Cutoffs for Cocaine and Heroin-Related Analytes Applied to an Addiction Medicine Setting: Important, Unanticipated Findings Using LC-MS/MS

By James G. Flood et al.

This paper describes studies with oral fluid cocaine and heroin-related testing using liquid chromatography-mass spectrometry. The authors had initiated oral fluid testing hoping that it would provide more accurate patient results. After six plus years of effort, the authors successfully introduced the new cocaine and heroin oral fluid tests. They observed surprising new findings that helped the new test be successful, such as the previously unknown predominance of cocaine, not the metabolite benzoylecgonine, in oral fluid many hours after actual cocaine use.