Clinical Chemistry

May 2017 Audio Summary

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ON THE COVER: Basil Doumas. Official records list Basil Doumas' date of birth as July 16, 1930, but only because his father altered the true date so that Doumas would have an extra year to pursue his studies before being drafted for military service. This minor alteration of the records played an important part in his future. Doumas obtained his college degree the day before he left to join the army. Fate continued to smile on Doumas and ultimately on the field of clinical chemistry. When he started in the field, the "standardization" and "harmonization" of methods was not part of the thinking of many clinical chemists. Doumas pioneered methods for accurately measuring bilirubin and important proteins. However, to many, the most notable thing about Doumas is his propensity for playing pranks. And that is the part of the story that you will need to read for yourself in our Inspiring Minds feature in this issue of *Clinical Chemistry.*

Utilization of Reflex Testing for Direct Bilirubin in the Early Recognition of Biliary Atresia
By Leo Lam, et al.

Direct bilirubin is increased from the early days of life in patients with biliary atresia, a life-threatening condition if untreated. The authors of this study examined the national database of patients with biliary atresia and found a substantial number of patients may have been diagnosed earlier if direct bilirubin was performed at the same time as total bilirubin. Laboratories in the Auckland region have therefore implemented reflex testing for direct bilirubin. The authors audited results from one hospital and one community laboratory and identified reflex testing to be cost-effective with minimal interruptions to hospital service delivery. These results demonstrate the role of laboratory initiated reflex testing for direct bilirubin in the recognition of biliary atresia.

Cross-sectional Analysis of AGE-CML, sRAGE, and esRAGE with Diabetes and Cardiometabolic Risk Factors in a Community-Based Cohort
By Stephanie J Loomis, et al.

Advanced glycation end products, abbreviated AGEs are considered central to diabetes, although associations in previous studies have been mixed. In a subsample of the Atherosclerosis Risk in Communities Study, the authors of this study evaluated associations between diabetes and cardiometabolic risk factors with three AGE-related biomarkers measured using the most commonly used ELISA assays: AGE-CML, sRAGE, and esRAGE. Adjusted models showed no significant differences by diabetes, but body mass index and C-reactive protein were associated with all three biomarkers. Black race, variants of the AGER gene, and kidney measures were strongly associated with lower levels of sRAGE and esRAGE. These results suggest that the ELISA assays are highly non-specific and may have limited value for diabetes research.

Quantifying the Release of Biomarkers of Myocardial Necrosis from Cardiac Myocytes and Intact Myocardium
By Jack Marjot, et al.

This paper examines the amount of myocardium that needs to undergo necrosis to increase troponin above decision-making cut-points. This question was addressed in-vitro using human and animal myocardium and isolated cardiomyocytes. A few tens of milligrams of heart tissue were found sufficient to increase systemic troponin concentrations to values above the 99th centile. This finding highlights the extreme sensitivity of the current high-sensitivity troponin assays, which detect necrosis beyond the resolution of any other technique.

Copeptin Associates with Cause-Specific Mortality in Patients with Impaired Renal Function: Results from the LURIC and the 4D Study
By Vera Krane, et al.

In kidney disease arginine vasopressin cannot act efficiently via renal V2-receptors. Vasopressin is up-regulated leading to augmented activation of V1a- and V1b-receptors. This upregulation might contribute to cardiovascular and infectious complications. The authors of this study evaluated copeptin, a vasopressin-surrogate, and mortality among 3131 and 1241 patients from the LURIC- and 4D-Studies, respectively, representing the whole spectrum of renal function. When expressed per standard deviation increase in copeptin, the risk of coronary, infectious, and all-cause mortality increased by 25, 30 and 15%, respectively, in patients with estimated glomerular filtration rates between 60 and 89 ml/min/1.73m2. Results were similar among patients with more advanced renal disease, but no significant associations were found in patients with normal renal function.

Distinguishing Intake of New Synthetic Cannabinoids, ADB-PINACA and 5F-ADB-PINACA, with Human Hepatocyte Metabolites and High Resolution Mass Spectrometry
By Jeremy Carlier, et al.

ADB-PINACA and 5-fluoro-ADB-PINACA are two of the newest synthetic cannabinoids, with high potency and reported adverse events. Metabolic, pharmacodynamic, and pharmacokinetic studies for these molecules are still lacking. Here the authors investigated the in vitro human metabolism of these two synthetic cannabinoids to identify major specific urinary markers for intake. The authors conducted human hepatocyte incubations and subsequent analysis via high resolution tandem mass spectrometry and metabolite identification data-mining software. They identified 19 and 12 major metabolites of ADB-PINACA and 5-fluoro-ADB-PINACA, respectively, and suggest several metabolites of these synthetic cannabinoids as optimal markers for their intake.

Selecting Statistical Quality Control Procedures for Limiting the Impact of Increases in Analytical Random Error on Patient Safety
By Martin Yago

This paper examines the selection of appropriate statistical QC procedures to limit the probability of harming patients due to the reporting of erroneous results arising from an increase in analytical random error. A statistical model was used to construct nomograms relating the increase in the number of erroneous patient results reported due to an increase in random error with the capability of the measurement procedure operating under different QC rules. These nomograms simplify the selection of statistical QC procedures for QC planning based on risk management.

Single-Stranded DNA Library Preparation Preferentially Enriches Short Maternal DNA in Maternal Plasma
By Joaquim S.L. Vong, et al.

Use of single-stranded DNA library preparation methods has been speculated to enrich cell-free fetal DNA in maternal plasma. The authors of this study compared two types of single-stranded DNA library preparation methods and a standard double-stranded DNA library method using samples from first and third trimester pregnancies. Unexpectedly, no significant enrichment was observed in the overall fetal fraction in maternal plasma collected in the first trimester. The single-stranded DNA library method instead enriched short maternal DNA in maternal plasma and showed inferior performance compared with double-stranded DNA library methods when applied to non-invasive prenatal testing for trisomy 21.