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On the cover this month: *Four-day-old baby boy relaxing under a blue wrap cloth*. Although most babies are born healthy, some have physiological or genetic abnormalities that can be life altering. This issue of *Clinical Chemistry* contains 3 articles that highlight the role of the clinical laboratory in the diagnosis and treatment of diseases of newborns and infants. These articles include a clinical case study dealing with an infant with persistent jaundice, a review of newborn screening for lysosomal storage diseases, and a research report of a multiplexed real-time PCR test for spinal muscular atrophy and severe combined immunodeficiency.

Increased Rheumatoid Factor and Deep Venous Thrombosis: 2 Cohort Studies of 54 628 Individuals from the General Population
By Christine Louise Meyer-Olesen, et al.

The authors of this study tested the hypothesis that increased concentrations of rheumatoid factor are associated with an increased risk of deep venous thrombosis in individuals without autoimmune rheumatic disease and never tested before. 54 628 participants from the general population without autoimmune rheumatic disease had rheumatoid factor concentrations measured and were subsequently followed for up to 32 years. Increased rheumatoid factor was associated with up to 3-fold increased long-term risk and up to 9-fold increased 1-year risk of deep venous thrombosis. These findings suggest that markedly increased rheumatoid factor concentrations could be considered as a thrombophilic condition.

Monitoring IgA Multiple Myeloma: Immunoglobulin Heavy/Light Chain Assays
By Jerry A. Katzmann, et al.

The heavy/light chain assay was described in 2009, but it has not been clear how this assay should be used by the clinical laboratory. In this manuscript the authors describe some of the clinical laboratory validation and document the ability of the heavy/light chain assay to replace the panel of serum protein electrophoresis, immunofixation, and immunoglobulin A quantification for monitoring IgA myeloma. Patients with monoclonal IgA proteins that migrate in the beta fraction and have no M-spike represent approximately 10% of all myeloma cases. The authors describe how the heavy/light chain assay will be useful for these patients.

Comparison of Cardiac Troponins I and T Measured with High-Sensitivity Methods for Evaluation of Prognosis in Atrial Fibrillation: An ARISTOTLE Substudy
By Ziad Hijazi, et al.

It is not known if the distributions of troponin I and troponin T data and the prognostic information they confer differ in patients with atrial fibrillation. This study investigated the distribution, determinants, and prognostic value of cardiac troponin I and troponin T concentrations in plasma samples obtained at baseline in 14 806 individuals with atrial fibrillation. The study findings demonstrate that troponin I and troponin T are measurable in a vast majority of patients with atrial fibrillation, although their correlation is only moderate. The risk of cardiovascular events is highest in patients with concentrations of both troponins above the median. However, when information from clinical risk factors is present, either troponin provides similar prognostic information.

Impact of Smoothing on Parameter Estimation in Quantitative DNA Amplification Experiments
By Andrej-Nikolai Spiess, et al.

This work investigated the effect of smoothing in quantitative PCR or qPCR data analysis. Smoothing is an integral part of virtually all qPCR data processing steps and thus it has fundamental importance in diagnostics. However, smoothers have been taken for granted without much concern for the adverse effects they may exert. The authors analyzed the impact of smoothers on the estimation of the quantification cycle and amplification efficiency. They showed that many commonly used smoothers introduce substantial bias in qPCR quantifications dependent on amplification efficiency. However, they also identified smoothers with beneficial properties that were independent of the amplification efficiency. These data indicate that smoothing and filtering approaches should not be part of an automatic process but should be carefully selected.

Sex-Specific Associations of Established and Emerging Cardiac Biomarkers with All-Cause Mortality in Older Adults: The ActiFE Study
By Dhayana Dallmeier, et al.

This paper investigated the association between N-terminal pro B-type natriuretic peptide as a marker for hemodynamic stress, and troponins T and I, measured by high-sensitivity assays, as markers for myocardial injury and 4-year total mortality in older people. All cardiac biomarkers were found to be independently associated with all-cause mortality in this cohort of 1422 older people. The authors also found differences in these associations between men and women that may provide new insights in the interpretation of these clinical biomarkers among adults aged 65 or older.

Quantitative Charge-Tags for Sterol and Oxysterol Analysis
By Peter J. Crick, et al.

In this study the authors describe the design of a new type of derivatization agent that improves sterol analysis by LC-MS and is appropriate for the diagnosis of inborn errors of bile acid and cholesterol biosynthesis. The derivatization agent includes stable isotopes so that relative quantification can be performed. The resulting quantitative charge tags can be used to profile over 100 cholesterol metabolites in a single LC-MS run from microliter volumes of plasma.

Newborn Blood Spot Screening Test Using Multiplexed Real-Time PCR to Simultaneously Screen for Spinal Muscular Atrophy and Severe Combined Immunodeficiency
By Jennifer L. Taylor, et al.

This report describes an approach for detecting spinal muscular atrophy by newborn bloodspot screening in the same assay used to detect severe combined immunodeficiency. The authors chose real-time PCR because of its recent assimilation into public health newborn bloodspot screening to detect severe combined immunodeficiency. The authors used a locked nucleic acid probe to achieve the required specificity for the survival of motor neuron or SMN1 gene. The assay was validated in clinical dried blood spot specimens, with perfect discrimination between normal, carrier, and affected SMN1 genotypes. Newborn screening laboratories already screening for severe combined immunodeficiency could screen for spinal muscular atrophy with no change in sample processing and little change in assay costs.

Digital Microfluidic Platform for the Detection of Rubella Infection and Immunity: A Proof of Concept
By Alphonsus Ng, et al.

Congenital rubella syndrome results in miscarriage and debilitating birth defects for more than 100 000 babies carried to term each year. In this proof of concept study, the authors developed a digital microfluidic system to enable rubella virus IgG and IgM immunoassays, relying on magnetic particles to capture analyte from the sample and chemiluminescence for detection. When applied to a commercial test panel of serum samples, the new system had 100% sensitivity and 100% specificity. This portable digital microfluidic system may represent a useful new tool for identification of patients at risk for congenital rubella syndrome in low-resource settings.