time. Thus, duplicate genetic testing often represents inappropriate test utilization that can contribute an unnecessary burden on the laboratory and health care system.
Objective: The purpose of our study is to determine the incidence of duplicate testing of in-house genetic testing offered at a large medical center, which includes cystic fibrosis, factor V Leiden, prothrombin G20210A, methylenetetrahydrofolate reductase (MTHFR) C677T, and MTHFR A1298C, and to develop a tool to identify and block duplicate testing.
Methods: We retrospectively analyzed internal laboratory databases of all cystic fibrosis (n = 36164), factor V Leiden (n = 3264), prothrombin G20210A (n = 2890), MTHFR C667T (n = 1451), and MTHFR A1293C (n = 1290) testing performed at the molecular pathology laboratory at a large medical center from either January 2010 or January 2014 to July 2019. We analyzed and cleaned the databases with the R programming language, and we developed a prototype web-based app to proactively identify duplicate test requests with the Shiny R package.
Results: From January 2010 to July 2019, 3535 (9.8%) of the 36164 cystic fibrosis tests performed were duplicate tests for 3257 unique patients. Of these duplicate cystic fibrosis tests, 2997 were repeated once in the same patient, 244 were repeated twice in the same patient, 14 were repeated three times in the same patient, and 2 were repeated four times in the same patient. From January 2014 to July 2019, 99 (3.0%) of the 3264 factor V Leiden tests, 86 (3.0%) of the 2890 prothrombin G20210A tests, 49 (3.4%) of the 1451 MTHFR C667T, and 46 (3.6%) of the 1290 MTHFR A1298C tests performed were duplicate tests.
We developed a proof-of-concept Shiny web-browser app that provides a user-friendly interface to determine if a patient has been previously tested in the molecular pathology lab. This app operates locally on a laboratory computer and uses spreadsheets automatically exported from the electronic medical record. These features allow for the app to be deployed quickly without needing to be integrated into the electronic medical record.
Conclusions: The results of this study indicate that unnecessary duplicate testing represents a small but significant proportion of genetic testing performed by the molecular pathology laboratory. Duplicate testing occurred more frequently with cystic fibrosis testing, which reflects its high volume at the medical center. Deployment of web-based apps using Shiny can provide straightforward and efficient tools for reducing duplicate tests.

Comparison of three serum androstenedione assays: the Siemens Immulite immunoassay, the Roche Elecsys immunoassay, and an LC-MS/MS assay

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Introduction: Serum androstenedione (ASD) is a useful biomarker in the diagnostic workup of hyperandrogenism, congenital adrenal hyperplasia, premature adrenarche, and polycystic ovary syndrome (PCOS). Recently, the Elecsys ASD assay (Roche Diagnostics), a competitive electrochemiluminescence immunoassay, became available in the US. Herein, the analytical and clinical performance of the Elecsys ASD assay was tested and compared with the Immulite assay (our current assay) and an LC-MS/MS assay (the gold standard) using deidentified residual patient specimens.
Method: In this study, the linearity, analytical measuring range (AMR), precision, and accuracy of the Elecsys ASD assay (cobas e602 analyzer) were tested. ASD from 40 deidentified residual serum/plasma samples was measured and compared between the Elecsys assay, the Immulite assay, and an LC-MS/MS assay. The reference intervals (RIs) provided by Roche for healthy male (0.280-1.52 ng/mL), healthy female (0.490-1.31 ng/mL), postmenopausal female (0.187-1.07 ng/mL), healthy children (<0.519 ng/mL), and patients with PCOS (0.645-3.47 ng/mL) were tested with at least 20 specimens, according to CLSI C28A3. Statistical analysis was performed using EP evaluator and R program.
Result and conclusion: The assay had a linear response across the AMR (0.3-10.0 ng/mL). The inter- and intra-assay coefficients of variation measured at multiple concentrations were less than 4.5% and 2.0%, respectively. The Elecsys ASD assay had an excellent correlation with the LC-MS/MS assay with a mean bias of -0.0542 ng/mL (-2%). The Immulite assay had a mean bias of 1.15 ng/mL (44%) and 1.22 ng/mL (32%) compared to the LC-MS/MS and Elecsys ASD assays, respectively. The Roche recommended RIs for healthy males and postmenopausal females were successfully verified in our patient population. However, the ASD concentrations for the healthy children were outside of the suggested RI, with concentrations up to 1.41 ng/mL. Therefore, the RIs for healthy children were adopted from RIs established using the same LC-MS/MS method used for method comparison. RI verification for the healthy female group also failed since many low ASD values were observed. Instead, a RI of < 1.30 ng/mL was established using 60 deidentified residual serum/plasma specimens. Finally, a separate RI for the PCOS group was not established since it may not provide useful clinical information due to the heterogeneity of the group. Unlike some published studies, hormone therapies such as oral contraceptive pills did not cause a significant decrease in ASD in patient specimens (p=0.4967). Overall, the Elecsys ASD assay has superior comparability to the LC-MS/MS assay than the Immulite assay. We were unable to verify the applicability of the RIs recommended by Roche for healthy females and children, warranting the need to establish or transfer them. When RI verification is challenging due to limited qualified

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specimens, transferring from an LC-MS/MS established RI is possible as long as the methods are comparable.

Heavy Chain Disease Reviewed on MALDI-TOF

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Heavy Chain Disease (HCD) is a group of rare B-cell proliferative disorders. Diagnosis depends on the detection of a truncated heavy chain with no associated light chain, often done by serum or urine immunofixation. This approach has been reported to have low specificity, since associated light chain bands are sometimes not visible and heavy chain bands can be mistaken for polyclonal bands. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) offers improved sensitivity in detecting monoclonal immunoglobulins. Truncation is thought to happen in the constant heavy chain (CH1) region, detected as a fragment of mass 27,000 Da on MALDI-TOF. Other mass patterns have not been reported in the literature. In this study, frozen serum samples from 8 heavy chain disease patients were analyzed by MALDI-TOF mass spectrometry. Spectra were reviewed on Mass-Fix software and visually inspected for monoclonal peaks. We detected two types of patterns for the IgG heavy chain disease. One pattern shows an IgG heavy chain with truncated mass (27,000 Da vs. 50,000 Da) and another in which the mass of the IgG heavy chain is greater than normal (65,000 Da). Follow-up work demonstrates that these are most likely dimers of truncated heavy chains. Thus, mass spectrometry-based immunofixation can provide new insights into heavy chain disease biology, mechanism, and progression, which are not identified by traditional diagnostic methods.

Discordantly Elevated Apolipoprotein B versus Low-Density Lipoprotein Cholesterol is Associated with Remnant Lipoproteins and Increased Cardiovascular Events

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Atherosclerotic cardiovascular disease is a result of low-density lipoprotein (LDL) particles becoming trapped in arterial walls and forming plaques which ultimately restrict blood-flow. LDL cholesterol (LDL-C) and apolipoprotein B (apoB) are highly correlated measures of plaque-causing LDL particles. Both have been shown to predict major adverse cardiac events (MACE). ApoB is also carried on remnant lipoproteins (RLP). RLP-cholesterol (RLP-C) is increasingly appreciated as a MACE risk-factor. This study aimed to define discordances between apoB and LDL-C in a large data set from a clinical reference laboratory. We then applied this definition to evaluate which measure predicted the risk of MACE in a patient cohort referred for coronary angiography with >10 years follow-up. LDL-C was measured by beta-quantification and RLP-C was defined as total cholesterol – LDL-C – HDL-C. Apo B discordance relative to LDL-C was determined by linear regression in a discovery cohort (n=17,203) using beta quantification. Discordance was defined by quartiles of the residual-apoB (expected–actual); discordant-low (<25th percentile), concordant (25th to 75th percentile) and discordant-high (>75th percentile). Associations with prevalence and incident of MACE were evaluated by odds-ratio and logistic regression. Risk of MACE was calculated based on the apoB-discordance and reported MACE events by several years follow up in a separate cohort (n=501). In the discovery cohort, age ranged from 18-95 years, 51% were female and mean (±SD) lipid values were: ApoB: 100.4 ± 30.0mg/dl, LDL-C: 121.7 ± 47.9mg/dl, and RLP-C: 17.2 ± 26.9mg/dl. Expected-apoB was described by the formula: (LDL-c X 0.6278 + 24.07, R=0.88). Residual-apoB (discordance) ranged from -1037 to 581.2 with a mean 0.01±18.6, and notably increased with triglyceride concentration (rho=0.65) and with RLP-C (rho=0.64), but was minimally influenced by apoB (rho=0.35) and LDL-C (rho=0.009) (p<0.001 all cases). In the clinical follow-up cohort, age ranged from 26-77 years, 42% were female, 64% were current/former smokers, and 28% were on lipid-lowering therapy. Mean (±SD) lipids were: apoB: 97.8 ± 20.9mg/dl, LDL-C: 124.6 ± 36.6mg/dl, and RLP-C: 34.9 ± 25.6mg/dl. Serum triglycerides among subjects discordant-low apoB, concordant and discordant-high apoB were 148mg/dL, 157mg/dL and 238mg/dL, respectively; similarly for RLP-C. A total of 192 events occurred during a mean of 9 years follow-up. Subjects with discordantly elevated apoB had a significantly higher incidence of MACE compared to those with concordant values (47% vs. 36%, p=0.03). There was no difference in MACE for subjects with discordantly low apoB (35% vs. 36%). These data support previous reports of an association between apoB and LDL-C and the superior performance of apoB when discordantly elevated. Our data expand on previous studies by applying an externally defined threshold for discordant-apoB. Our data indicate that triglycerides, RLP-C are associated with discordances and MACE.

Assessment of Clinical Ordering Practices of Phosphatidylethanol Monitoring for Alcohol Use at a Large Academic Medical Center

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Objectives: Phosphatidylethanol (PEth) has emerged as a specific biomarker for alcohol use with superior diagnostic

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