To the Editor.—Interference from lipemia can significantly impede accurate analysis of a variety of laboratory tests independent of instrumentation or manufacturer. Conventional treatment of lipemia involves ultracentrifugation of specimens at approximately 199 000g to pellet and clarify interfering lipids. Although effective, this approach requires additional instrumentation, which may be costly for smaller, satellite laboratories offering a limited testing menu. Triaging lipemic samples to larger reference laboratories or core facilities may be impractical because of extended turnaround times and specimen rejection of lipemic samples, thus hindering patient care.

Recently, our institution evaluated a lipid-precipitating, nonionic-cyclodextrin polymer, LipoClear (Statspin, Westwood, Massachusetts) as an alternative to ultracentrifugation in satellite laboratories as a means of reducing cost and improving turnaround time. Plasma and serum samples (n = 40) with grossly elevated lipemia (≥3+ ) were collected and refrigerated before analysis. Lipemia indices before treatment ranged from 3 to more than 10 (median = 6+). Specimens were split and treated to conventional ultracentrifugation (15 minutes at 199 000g) or with LipoClear (5 minute incubation of 500 μL of sample and 100 μL of LipoClear, followed by 7 minutes at 3461 g). Clarified specimens were transferred to new tubes and analyzed on a Beckman Coulter DxC800 (Fullerton, California).

LipoClear-treated specimens showed good agreement with paired ultracentrifuged specimens for all assays tested: sodium, potassium, chloride, carbon dioxide, calcium, glucose, blood urea nitrogen, total protein, albumin, alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, total bilirubin, phosphorous, creatinine, and creatine kinase. Linear regression analysis demonstrated acceptable performance across clinical decision points for all analytes. Correlation coefficients ranged from R = 0.92 to R = 0.99 for all analytes, except sodium and total protein, whose coefficients were R = 0.90. Sodium demonstrated a mean positive bias of 3.6 mEq/L (mmol/L) using LipoClear, compared with ultracentrifugation (Figure 1, A and B). This was considered within the limits of acceptability for the assigned total error budget of ±4 mEq/L (mmol/L) at pertinent medical decision points. Total protein demonstrated a mean
negative bias of 0.65 (g/dL) using LipoClear, compared with ultracentrifugation. Previous work has compared preanalyte and postanalyte measurements on the Beckman Synchron LX-20, after artificial spiking of nonlipemic samples with the synthetic lipid Intralipid (Uppsala, Sweden). In this study, no discordance between recovery with ultracentrifugation and LipoClear was observed with sodium or total protein, highlighting potential limitations for Intralipid as a universal substitute for assessing endogenous lipemic interferences. Additionally, 78% of LipoClear-treated samples showed lower lipemia indices after treatment than did their paired ultracentrifuged specimens, suggesting a more-complete removal of interfering lipids. The results here are limited to performance on the DxC800, and it is the responsibility of the laboratory to validate any preanalytic specimen manipulation not covered in the manufacturer’s instructions for use.

Analytic performance aside, implementation of LipoClear in satellite laboratories reduced cost and drastically improved turnaround time for reporting lipemic specimens. Process mapping identified 11 steps necessary for dealing with lipemic specimens before chemotherapy infusion for our oncology clinic (Figure 2). Before any clinical procedure, an additional waiting time of at least 2 hours was not uncommon because of courier pickup, delivery, ultracentrifugation at the off-site laboratory, and result reporting. Incorporation of the onsite treatment of lipemia reduced the number of steps from 11 to 7 and added only 15 minutes compared with normal specimens. The economic barrier of approximately US $14,000 for purchasing ultracentrifuges for every satellite laboratory, as well as the need for a dedicated air supply for their operations, had previously prevented onsite treatment of affected specimens. Incorporation of this protocol returned results for lipemic specimens 87% faster and reduced cost 3-fold. Collectively, the elimination of costly equipment and courier fees, coupled with a shorter turnaround time, added value for both our satellite laboratories and for our patients.

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Letters to the Editor

CONFIRMATORY TESTING OF URINE KETONES AND BILIRUBIN: STILL NECESSARY?

To the Editor.—Urinalysis is a useful tool in diagnosis, screening, and monitoring the progress of diseases.1 However, laboratory practice is inconsistent in the use of urine confirmatory tests for the presence of ketones and bilirubin in urine. Thus, we recently conducted a study and intended to standardize this issue.

Urine ketone level was measured using a nitroprusside reaction and bilirubin was measured by the diazo method on an Aution Max AX-4280 automated urine chemistry analyzer (Iris Diagnostics, Chatsworth, California). Urine ketones were confirmed with Acetest and bilirubin was confirmed with Ictotest (Bayer Corp, Elkhart, Indiana). Of 492 urine samples analyzed for ketones on the AX-4280, 42 (8.54%) were positive for ketones. Acetest confirmed 35 of the 42 ketone-positive samples as ketone positive (Table). Most of the discrepancies between urinalysis and Acetest results were seen at 10 mg/dL on the AX-4280. Of 4270 urine samples analyzed for bilirubin on the AX-4280, 108 samples were positive for bilirubin (2.53%) and 107 of those samples were confirmed to be bilirubin positive by Ictotest (Table). A survey was also conducted showing that 13 of the 25 responding laboratories were still doing confirmatory testing for bilirubin by Ictotest (52%). Similarly, 2 of 8 responding laboratories were still using Acetest to confirm urine ketones.

The confirmatory testing was historically performed to confirm results obtained from the urine dipstick. Substantial improvements in the sensitivity and specificity of automated semiquantitative analyzers have dramatically reduced the necessity of confirmatory testing. We believe that there is no rationale for continuing these confirmatory tests, for the following reasons:

1. Currently there is no guideline on whether confirmatory testing needs to be done for urine ketones or bilirubin. The Clinical and Laboratory Standards Institute has stated that “many of the historical confirmatory chemical urinalysis tests such as the sulfosalicylic acid (SSA) test for protein, the tablet test for ketones, and the tablet test for bilirubin may not be relevant to current laboratory practice.”2 The College of American Pathologists does not require these confirmations and suggests that users follow the manufacturer’s recommendations.
2. Our survey findings suggest that most laboratories have discontinued or will soon discontinue these confirmatory tests.
3. Our data show that confirmatory tests results agree well with those from automated urinalysis with exception of the reading of trace ketonuria by Acetest.3 Acetest itself is less sensitive and more subjective compared with automated urinalysis using the AX-4280.
4. Detection of urine ketones by confirmatory testing does not