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Evaluation of Leukocyte and Bacterial Interference in Point-of-Care Human Chorionic Gonadotropin Tests

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We read with interest the Letter to the Editor by Jao et al. [1] which reported false positive results using the point-of-care (POC) One Step Pregnancy Test device (ACON Laboratories Inc., San Diego, CA, USA). The authors determined that false positive results occurred when the concentration of white blood cells (WBCs) in a urine specimen exceeded 0.4×10^9 cells/L.

We recently observed several false-positive human chorionic gonadotropin (hCG) results using the POC hCG Combo Rapid Test (Cardinal Health, Waukegan, IL, USA). We observed that most of our false positive specimens were in patients with evidence of urinary tract infection (UTI) and pyuria; with this information, and in the context of the findings by Jao et al. [1] that WBCs may result in false positive hCG assays, we evaluated the effect of WBCs or bacteria in urine on the analytical performance characteristics of both devices.

Two buffy coat preparations were created using pooled whole blood from 25 patients. The buffy coat preparations were analyzed using the Coulter LH 750 Hematology Analyzer (Beckman Coulter, Brea, CA, USA) to assess the purity of the preparation. WBCs were prepared on two separate occasions and the total WBC counts of the pools were 57.5×10^9/L and 200×10^9/L. These WBC preparations were then diluted into urine from a male patient at six different WBC concentrations (0.1×10^9, 0.4×10^9, 1.0×10^9, 5.0×10^9, 10.0×10^9, and 21.0×10^9/L) including and exceeding the concentration used by Jao et al. [1]. The urine was then tested on both the hCG One Step and the hCG Combo Rapid test according to the manufactures' recommendations. All specimens were negative on both devices.

The explanation for the different results observed in the study by Jao et al. [1] and the current study are unclear. Jao et al. [1] do not describe the source of their WBC preparation, it is unknown if it is from one patient or multiple patients, and the WBC differential is also unknown. It is possible that differences in these parameters could explain the discrepancy. With the knowledge that most of our patients with false positive results had evidence of UTI, and knowing that *Escherichia coli* is the most common cause of UTI in the outpatient setting, we wondered if *E. coli* specifically might account for the false positive results. To test this hypothesis, we made logarithmic dilutions (10^7 colony forming units [CFU]/mL, 10^6 CFU/mL and 10^5 CFU/mL) of a clinical isolate of uropathogenic *E. coli* into sterile urine from a male patient and tested these samples on both devices; all tests yielded negative results.

To account for the fact that addition of *E. coli* and/or WBCs to sterile urine might not accurately replicate the matrix of a clinical specimen from a patient with UTI, we then tested 10 urine specimens from unique, female patients that were culture positive for *E. coli* (>50,000 colonies/mL) and 5 additional urine specimens that were submitted from outpatients to the microbiology laboratory for culture for presumed UTI. All of these speci-

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mens, when tested with the hCG Combo Rapid Test, also gave negative results.

A recent study by Snyder et al. [2] reported that high WBC concentrations resulted in falsely increased serum hCG concentrations using the Beckman Coulter Access Total βhCG on the UniCel DxI (Beckman Coulter, Chaska, MN, USA). According to the authors, the false positive results may be attributed to leukocyte alkaline phosphatase reacting with the conjugate that is used in those immunoassays. However, both POC devices used in this particular study use colloidal gold as the color conjugate, hence leukocyte alkaline phosphatase should not result in this specific interference. Based on the information in this study, we feel there is inadequate evidence at this time to conclude that false-positive hCG results, in either the One Step Pregnancy Test device or the hCG Combo Rapid Test, can be attributed to elevated WBC concentrations in the urine. However, we continue to see false positive results that suggest the presence of a yet unidentified interfering substance.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported for JVM or C-ADB. AMG has served as a consultant and expert witness for Church and Dwight Inc.

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