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Response to Letter to the Editor: "Assay-Specific Spurious ACTH Results Lead to Misdiagnosis, Unnecessary Testing, and Surgical Misadventure—A Case Series"

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While we agree that all immunoassays are susceptible to interferences, we do not agree that it is necessarily "rare" with respect to the Seimens Immulite adrenocorticotropic (ACTH) assay. In fact, we did not use the term "rare" in our article [1, 2] and dispute this inference by Drs. Altawallbeh and Karger. Although interferences in other ACTH assays may be rare, it is our opinion that our findings may be the tip of the iceberg with respect to the Immulite ACTH assay. We stated the following on page 769 of our article, "Since the assembly of our case series, multiple other instances of diagnostic confusion related to this [Immulite ACTH] assay have been brought to our attention, many of which resulted in prolonged and unnecessary endocrine testing and procedures for suspected Cushing syndrome, creating a potential patient safety problem" [1]. We want to again draw the reader's attention to the case series by Donegan et al who presented 12 patients who were similar to ours [3].

A recent study by Shi et al used intact ACTH (iACTH) measured by liquid chromatography with tandem mass spectrometry (LC-MS/MS) as an arbiter of clinically discordant results [4] and stated the following on page 1403: "Analysis of the current set of immunoassay discordant samples revealed that the Roche [Cobas ACTH [5]] results were highly positively correlated with iACTH measured by LC-MS/MS, whereas the Siemens results were only modestly positively correlated with iACTH." We have no way of knowing the number of patients worldwide whose care has been compromised by erroneous results due to ACTH immunoassay interference. This would require a comprehensive, split-sample study. However, examination of Figure 2A in Shi et al shows that 3 out of 78 (~4%) blood samples collected for routine clinical measurements had appropriate Roche Cobas ACTH results but discordant Immulite ACTH results that were resolved using LC-MS/MS [[4], Fig. 3].

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We stand by our conclusions [1]. We do agree that a clinical result for any laboratory measurement that does not agree with the patient's clinical presentation or other biochemical results should be repeated and further evaluated using an alternate method of measurement.

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Additional Information

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