Commentary

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The measurement of cyclosporin A (CsA) concentrations has long been a challenge, owing to factors such as the large number of metabolites. Even highly specific liquid chromatography–tandem mass spectrometry assays can have analytical problems. The case reported by Peter et al. of a human antimouse antibody (HAMA) causing interference within a CsA immunoassay illustrates the insidious nature of this type of interference. It was not until 6 weeks after the discontinuation of CsA therapy that the higher-than-expected concentration was detected in this case. How much this HAMA interference contributed to the measured concentration in this patient while she was still receiving the drug is unknown; however, that it did is entirely conceivable. The approach to evaluating this interference also demonstrates the effort that is often expended to confirm the presence and identity of an interfering substance. I do not view this effort as just an academic exercise. HAMA confirmation has important implications for other testing of this patient and perhaps the testing of other patients. The authors were fortunate to be able to confirm the presence of a HAMA by blocking with heterophile antibodies. This treatment is not always successful, despite the presence of a HAMA. The widespread use of immunoassays and the increasing use of antibody-based therapeutics will most likely lead to more HAMA problems, not fewer, even with the efforts to humanize therapeutic antibodies. Unfortunately, most HAMA interferences are likely missed during the routine practice of medicine. Laboratorians must therefore maintain vigilance for this important and potentially life-threatening problem. Effective communication with laboratory clients is also critical, because the healthcare providers directly caring for the patient are likely be the first to notice the problem when the result does not fit with their clinical impression.

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