Commentary

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This case highlights the importance of understanding the limitations of immunoassays in the emergent setting. The number of deaths due to drug overdose continue to rise, and many institutions rely on urine drug testing by immunoassay to support the diagnosis and management of patients presenting with potential overdose *(1)*. Urine is typically the specimen of choice because drugs are present in higher concentrations and the collection process is noninvasive. However, urine results may not explain the current situation, as drugs and/or metabolites can be present for several days. False-negative results can also be obtained immediately after drug ingestion or if the patient's urine is dilute. Therefore, serum testing may be necessary to confirm an overdose.

Although immunoassays are rapid, relatively inexpensive, and easy to automate, there are some limitations, including poor analytical sensitivity and specificity *(2)*. Most benzodiazepine immunoassays are designed to detect older benzodiazepines, such as diazepam and its metabolites, and have variable cross-reactivity with newer benzodiazepines such as lorazepam, clonazepam, and alprazolam and their metabolites. As the authors illustrate, cross-reactivity with 7-aminoclonazepam, the primary metabolite found in urine, is poor, and false-negative results can be obtained even in overdose situations. For this reason, laboratories may offer definitive testing by mass spectrometry to overcome the limitations of immunoassays; however, the turnaround time should be considered.

Laboratories should educate their clinicians on the limitations of their immunoassays. At a minimum, there should be communication between the laboratory and the end-users, and the clinicians should have laboratory contacts when questions arise. The laboratory could also provide comments attached to results that remind clinicians of the limitations and/or create an online resource to assist with result interpretation. In this case, the clinicians appropriately managed the patient with flumazenil on the basis of the clinical presentation. However, the outcome could have been devastating if the possibility of a false-negative result was not considered.

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Commentary

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This case highlights 2 topics in intoxication management: pitfalls of the urine benzodiazepine immunoassay and controversies over administering flumazenil for undifferentiated coma.

Urine benzodiazepine immunoassays are calibrated against a specific metabolite, thus limiting their analytical sensitivity and resulting in frequent false-negative results, leading to misdiagnosing benzodiazepine intoxication as another process. However, the reciprocal situation of a positive result that is due to use and not intoxication is potentially more dangerous. Urine immunoassays were designed for workplace drug testing; they are qualitative and targeted toward metabolites to increase the window of detection. A positive assay result may anchor decision-making away from treating an intoxication that requires antidotal therapy, such as acetaminophen or tricyclic an-

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