

## Commentary on "Delayed Norfentanyl Clearance during Pregnancy"

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We present a case of a pregnant woman with opioid use disorder and prolonged norfentanyl clearance not previously described in the medical literature. Circa 2012, illicitly manufactured fentanyl swiftly infiltrated the US opioid drug trade resulting in a devastating spike in overdose mortality; the ramifications of which we still suffer. This rapid shift in the illicit opioid market caught consumers, addiction providers and health officials off guard. Unaware of fentanyl's infiltration of the opioid street supply and its potency, consumers suffered unintentional overdose fatalities. As is often the case, the medical system was out paced by the ever shifting and evolving street drug trade and routine urine drug tests did not include fentanyl.

Medical facilities were not prepared to test for fentanyl ingestion rendering providers unable to warn clients against morbidity of future fentanyl use. Today, many facilities have yet to adopt routine testing to detect fentanyl and its inactive metabolite, nor fentanyl. Providers equipped with the infrastructure to test for fentanyl are able to identify the compound in urine samples but the science of mapping the trajectory of human metabolism and renal clearance continues to lag behind identification. Clinical assumption of fentanyl clearance mirroring the 72 hour duration of less potent opioids has been false. Fentanyl clearance and the factors effecting duration of clearance remain unknown.

Further research on impact of genetic and physiologic variants, including pregnancy, on fentanyl clearance is needed. In this window of scientific uncertainty of fentanyl pharmacokinetics, providers must remain vigilant to avoid errors of assumption.

Clinicians who order urine drug tests for their clients in recovery hold a powerful responsibility for accurate interpretation of the results. The magnitude of such responsibility is most palpable in cases of child custody in which medical laboratory results are entered as legal evidence. If an error in the medical interpretation of such evidence, by either limitations of the science or provider knowledge, is propagated as fact into the court system, we have failed our moral duty as clinicians, scientists and patient advocates.

As an Obstetrician and Addiction Medicine Specialist, I stand at the crossroads of providing dignified recovery treatment for pregnant persons and communicating her recovery course to the family court system. Healthcare standards and cultural ideals in the US expect all pregnant women to engage in prenatal care. In kind, pregnant women with substance use disorders are pressured internally and externally to seek recovery treatment during gestation. The result of such influences motivates the majority women with SUD to seek recovery treatment during pregnancy.

Maternal and fetal outcomes are markedly improved with barrierfree access to addiction treatment, including MOUD, for pregnant women. Women present for care in the hopes of creating a new life for her and her baby; a desire to start anew and build a healthy family. As we enter this patient-provider relationship, it is imperative both parties understand the importance of transparency and the regional regulations for mandated reporting of suspected child abuse or neglect. Providers must understand their role in mandated reporting and extend their expertise in accurate translation and interpretation of laboratory values and urine drug testing results.

The world of urine drug immunoassays can be confusing and complicated to decipher. Even for medical providers who commonly order urine drug tests, the results are not always selfevident. Therefore, the expert interpretation of test results required in custody cases should not be the sole responsibility of non-medical personnel. Our case report of pregnant women whose urine norfentanyl level, fentanyl's inactive metabolite, remained detectible (positive) for 72 days following last fentanyl ingestion.

To the unversed, this might appear as evidence of continued fentanyl use through her pregnancy calling onto question her treatment efficacy, her engagement in recovery care, her reliability and her honesty. Inaccurate interpretation of these results would have jeopardized maintaining maternal custody at delivery. Our case report outlines her protracted clearance of norfentanyl with quantitative analyses allowing for the evidencebased identification of delayed norfentanyl clearance and its distinction from continued fentanyl use or relapse.

## GOALS IN SUBMITTING FOR PUBLICATION

• To highlight this previously un-reported phenomenon.

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- To encourage further research on fentanyl clearance in pregnancy
- To educate both medical and legal professionals caring for pregnant women with opioid use disorder.
- To prevent other women in similar situations from unwarranted custody disruptions.

The urgent message of this case begs the medical-legal community to ensure our utilization of urine drug testing and the interpretation of results are ethically implemented and accurately interpreted.