

Blood levels of common antiepileptic drugs drop during pregnancy, causing breakthrough seizures

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Blood levels of many commonly used antiepileptic drugs drop dramatically with the onset of pregnancy, report researchers from the University of Pittsburgh and the University of Minnesota today in *JAMA*

Neurology.

The findings, collected as part of the multicenter study Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD), explain why many people with [epilepsy](#) start experiencing breakthrough seizures after conception, reinforcing the need to proactively increase doses of certain antiseizure medications and closely monitor [blood levels](#) over the course of [pregnancy](#).

When it comes to epilepsy, maintaining a fine-tuned [medication](#) regime is critical. Some people mistakenly believe that changes in the drugs' blood concentration won't occur until after 20 weeks of pregnancy, but our study shows how important it is to start monitoring and adjusting patients' medication dosages early on," said lead author Page Pennell, M.D., chair of neurology at Pitt and the principal investigator on the MONEAD trial. "Nearly half of all pregnancies in the United States are unplanned, so it is important to ensure that doctors have a clear picture of each patient's baseline drug level even if they are not trying to conceive."

Epilepsy is a life-altering neurological condition that affects children and adults alike, and two-thirds of cases do not have a known cause. In people with epilepsy, nerve cells in the brain are hyper-reactive, causing them to change the pattern of their electrical activity and become spontaneously active, millions of cells at a time. In people with epilepsy, that synchronous activation is manifested in seizures, which can make a person become disoriented, lose consciousness and, in some cases, experience limb movements or rigidity.

Clinical management of epilepsy has had a fraught medical history, compounded by myths and stigma over the centuries. Many people with epilepsy go undiagnosed or under-treated. Even though [epileptic seizures](#) can often be successfully controlled with medications, the first-

generation drugs had a slew of dangerous side effects and were contraindicated for people who are trying to conceive.

Since then, safer medications have entered the U.S. market and become widely available, but clinicians started noticing a new problem—patients whose epilepsy was successfully managed with medications started having seizures soon after becoming pregnant.

"Identifying which antiseizure medications may have changes in concentrations and at what point in pregnancy those changes occur is important for determining which patients may need to be monitored more closely during pregnancy and after delivery," said senior author Angela Birnbaum, Ph.D., professor of experimental and clinical pharmacology at the University of Minnesota.

To get to the bottom of the mystery, Pennell and colleagues launched a study to analyze blood concentrations of 10 commonly used antiseizure drugs and compare them across different stages of pregnancy and after childbirth.

The study found that blood levels of seven out of 10 of the medications they examined dropped dramatically—from 29.7% for lacosamide, a commonly prescribed anticonvulsant, and up to 56.4% for lamotrigine.

In addition, the researchers noted that the drop in the drugs' blood concentration occurred mere days after conception, long before most women have their first prenatal visit and before the pregnancy showed itself physically.

"Until now, we knew very little about how becoming pregnant impacted blood levels of most anti-epileptic medications," said Vicky Whittemore, Ph.D., program director at the National Institute of Neurological Disorders and Stroke (NINDS). "This study lays the groundwork for a

larger goal of the MONEAD study, which is to improve outcomes in women with epilepsy by better managing their medications over the course of pregnancy."

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