In this issue of Pediatrics, Bateman et al\(^1\) have elegantly convinced readers that infants of mothers prescribed \(\beta\)-blockers in late pregnancy, in a large American database, have a significantly elevated risk (4.3\%) of neonatal hypoglycemia, with an adjusted odds ratio of 1.68. This finding is important because \(\beta\)-blockers are used commonly to treat hypertensive orders in pregnancy, and in Bateman et al’s study >10,000 women, 0.5\% of pregnancies, delivering between 2003 and 2007 were exposed to \(\beta\)-blockers at the time of delivery. Their results are physiologically plausible because \(\beta\)-blockers cross the placenta, and the resultant sympathetic blockade could be expected to lead to hypoglycemia, which may be asymptomatic. Screening for hypoglycemia appears to be the natural conclusion. But should we?

The accepted definition of hypoglycemia at the time of this study was a blood glucose level \(\leq 45\) mg/dL (\(\leq 2.6\) mmol/L).\(^2\) The authors verified the electronic diagnostic codes by a random sampling of charts for a low blood glucose level or treatment with intravenous glucose or increased feeds. Whole blood glucose values are 15\% lower than serum samples, and variances in sampling, collection, and analytic methods can also affect glucose values.\(^3\) Unfortunately, our confidence in \(\leq 45\) mg/dL in the asymptomatic neonate as the threshold for treatment to avoid brain energy depletion and long-term developmental sequelae is faltering. The use of continuous interstitial glucose monitoring of at-risk neonates in the Children With Hypoglycemia and Their Later Development study group\(^4\) showed that 23\% of neonates with no documented hypoglycemia on blood glucose screening had \(\geq 1\) hypoglycemic episode on continuous monitoring. The severity, frequency, and duration of hypoglycemic episodes had no effect on adverse neuropsychometric or sensory outcomes, targeted to detect sequelae of hypoglycemic brain injury at 2 years of age. Approximately one-third of children had a developmental delay. Although it is clear that glucose is an important energy source for the brain, at this time there is no evidence to identify a blood glucose threshold associated with brain injury. The tolerance for hypoglycemia is affected by alternative sources of fuel, such as ketones and lactate. Many factors must be considered in the interpretation of a low blood glucose value.

McKinlay et al’s\(^4\) findings that greater fluctuation in glycemic control was associated with cognitive delay and that early steep increases in interstitial glucose were associated with neurosensory impairment raise a new concern that rapid correction of hypoglycemia may be harmful. Without convincing evidence that intervention for asymptomatic hypoglycemia is safe and effective, the potential harms of prolonged hospital stay or increased level of care, iatrogenic harm, heel lance–associated pain, and the cost of testing must be considered.

When evaluated according to Wilson and Jungner’s criteria,\(^5\) screening for neonatal hypoglycemia does not meet the following criteria: the natural history of the condition is understood, there is a test that is easy to interpret, and the diagnosis and treatment are...
cost effective. There is clearly a need for better evidence for the screening and management of neonatal hypoglycemia for both currently recommended conditions and after antenatal exposure to β-blockers.

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Screening for Neonatal Hypoglycemia After Fetal Exposure to β-Blockers
Anne Synnes
Pediatrics 2016;138;
DOI: 10.1542/peds.2016-1691 originally published online August 30, 2016;

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