CORRESPONDENCE

Zika Virus

TO THE EDITOR: Petersen et al. (April 21 issue) provide a detailed review of Zika virus. We have some concern regarding diagnostic criteria for microcephaly in fetuses and newborns exposed to the virus. According to the Centers for Disease Control and Prevention (CDC) recommendation that microcephaly should be defined as an occipitofrontal circumference below the third percentile, nearly 3% of newborns would be categorized as having microcephaly. In Brazil, where there are 3 million live births per year, the application of this definition...
would result in nearly 90,000 infants being labeled as having microcephaly — a far greater number than any studies to date would indicate. The comparable number in the United States would not be 2 to 12 cases per 10,000 live births, as noted in the article, but rather 3% of 4 million live births, or 120,000 newborns. The “benchmark” of an average of 6 cases per 10,000 live births in the United States is based on the most commonly used criterion of 3 SD from the mean, which would encompass 0.27% of newborns. A comparison of prevalence with the use of such radically different criteria will lead to grossly inappropriate conclusions and hysteria among pregnant patients. Unfortunately, this error has been repeated in press releases and needs to be corrected.

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TO THE EDITOR: In their review article, Petersen and colleagues from the CDC describe updated geographic projections for the distribution of Aedes aegypti and A. albopictus mosquitoes in the United States. A map based on data from the CDC indicates the potential presence of A. aegypti in New York City. However, support for the expanded geographic distribution of the mosquito is limited to a single study that relied on mathematical modeling of meteorologic conditions as a surrogate for detecting A. aegypti.

Since West Nile virus first entered the Western Hemisphere in 1999, the New York City Health Department has conducted comprehensive annual mosquito surveillance to guide mosquito control. From 2006 through 2015, we trapped and tested more than 1.2 million mosquitoes; several aedes species were found, but none were A. aegypti. In addition, after years of investigating hundreds of cases of human infection with dengue virus, and more recently chikungunya virus, local mosquito transmission of either virus has not been detected. These findings currently suggest a low likelihood of A. aegypti transmission of Zika virus in New York City.

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THE AUTHORs REPLY: In the United States, where percentile growth charts are preferred for assessing growth in pediatric health care, the third-percentile cutoff point for microcephaly is of practical usefulness, since this is the lowest designation on commonly available charts. FitzSimmons and Shah correctly state that infants at the tail end of the distribution of a percentile-based assessment of growth may be identified as being potentially abnormal. However, on the basis of birth-defects surveillance systems in the United States, 2 to 12 infants per 10,000 live births receive a diagnosis of microcephaly; thus, we may conclude that less than 3% of infants are receiving this diagnosis.

Given our limited understanding of the full spectrum of adverse outcomes associated with congenital Zika virus infection, CDC guidance recommends careful evaluation of infants who have a head circumference below the third percentile for gestational age and sex. However, the infant’s full clinical picture rather than the head circumference alone should dictate the intensity of follow-up and the ultimate clinical diagnosis of microcephaly. For example, there would be less concern about the possibility of underlying brain abnormalities in an otherwise healthy newborn who had a head circumference at the third percentile and a proportionally small birth weight and length than in a newborn who had a similar circumference but was at the fifth percentile for birth length and weight.
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Interference of New Drugs with Compatibility Testing for Blood Transfusion

TO THE EDITOR: New drugs may have important yet underappreciated clinical consequences in patients requiring blood transfusion. Interference with routine methods for compatibility testing for blood transfusion puts patients at risk for delays in receiving compatible blood. Even if laboratory methods are developed to circumvent the drug-related artifacts, it takes time to establish them in general laboratories.

Daratumumab (a monoclonal antibody that binds with high affinity to the CD38 molecule; manufactured by Janssen), which was recently approved by the Food and Drug Administration as a therapy for multiple myeloma, provides an illustrative case. Once enrollment in the phase 1–2 trial began, staff at the trial site quickly observed that daratumumab consistently interfered with routine blood-compatibility testing. Standard serologic methods to eliminate pan-reactive antibodies failed to resolve the interference, at times delaying needed blood transfusions for patients treated with daratumumab.

It was eventually shown that daratumumab in patients’ plasma directly binds to CD38 on reagent red cells used in the blood bank, causing the false positive antibody screens. A dithiothreitol-based method to eliminate the interference was discovered in an investigator-initiated study and was later shown to be both effective and widely generalizable in a multicenter international study performed by the Biomedical Excellence for Safer Transfusion (BEST) Collaborative (data not shown); both studies were sponsored by Janssen. A neutralization method with the use of an anti-daratumumab idiotype has shown promise; however, the antiidiotype method is