Congenital Zika Virus Infection: A Developmental-Behavioral Perspective

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Zika virus has captured the world's attention. It seems as if every day we learn more about the virus. Information about Zika virus pervades our media, from television to social media feeds. However, the focal point of scientific and media inquiry has been *congenital* Zika virus infection and microcephaly. Heightened awareness of this condition has changed the way people live their lives—from travel planning, to reproductive decisions, to the care of pregnant women, to blood and tissue donation.[1–3]

Zika virus is not the first infectious teratogen known to impact neurologic function and overall development. In fact, Zika virus is one in a long line of agents, including rubella, HIV, *Toxoplasma*, *Treponema*, varicella, and cytomegalovirus, that can result in lasting effects on the brain. While prenatal infection with some of these agents has become less common in the United States due to public health interventions including but not limited to immunization, they continue to cause significant morbidity in other parts of the world. While many of us care for children with autism spectrum disorder, some may not know that a constellation of findings, including deafness, cataracts, cardiac defects, and intellectual disability, termed congenital rubella syndrome has also been linked to the development of autism.[4] In sum, the link between prenatal infection and developmental manifestations is not a new observation but one that has been known for decades.

We feel that it is important to comment on congenital Zika virus infection, at this time, to summarize what is known and what is unknown about this condition, with a particular emphasis on what the Zika outbreak means for providers in Developmental-Behavioral Pediatrics. In addition, While many medical societies have already weighed in on congenital Zika virus infection, it is important to add the voice and unique insights of Developmental-Behavioral Pediatrics as a stakeholder in the conversation. Our longitudinal perspective allows us to foresee potential challenges and take steps to prepare, as a field, to meet the developmental needs of children affected by congenital Zika virus infection. From this viewpoint, we also introduce suggestions for clinical practice in caring for children who may be affected by this condition.

In the mass media, we are confronted by dramatic photos of infants with microcephaly, clearly illustrating the potentially devastating impact of Zika virus on the developing brain. It is obvious that these severely affected infants will experience significant developmental challenges. However, it is important for the field of Developmental-Behavioral Pediatrics to recognize that Zika virus is a teratogen with potential consequences far beyond microcephaly alone. Ultrasound findings associated with congenital Zika virus infection include brain atrophy, ventricular enlargement, intracranial calcifications, ocular defects, joint contractures/arthrogyposis, hydrops fetalis, agenesis of the corpus callosum, vermian agenesis, agenesis of the thalami, cataracts, thin cerebral mantle, and intrauterine growth restriction.[5] Recent estimates suggest that if a woman is infected in the first trimester, the risk of her fetus developing microcephaly ranges from 1% to 13%.[6] Children with microcephaly therefore represent only a fraction of the total population of children affected in one way or the other by congenital Zika virus. In our field, we treat many patients who have clearly impaired functioning, for example, children with autism spectrum disorder, but have normal brain magnetic resonance imaging (MRI). Now, a group of children are being born with demonstrable brain findings. This leads us to ask, "How will these children function?" It also raises questions about the effects of Zika virus in children without head circumference or MRI changes, but with potentially more subtle brain alterations that affect function, but cannot be detected by an MRI.

Endemic Zika virus has been detected in tropical and subtropical regions of the world, including part of the southern United States. But, in the age of inexpensive,

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ready travel, Zika has truly become a global concern. As we write this commentary, Zika virus infection has been detected in 49 states and Washington DC.[7] Most of identified Zika cases in the United States have involved international travel.[7] However, the discovery that Zika virus can be sexually transmitted adds an additional mechanism for viral spread.[8,9] It is easy to foresee that children with congenital Zika virus infection will be presenting to all of our developmental centers in the near future. It is less a question of "if," but more a question of "when" and "how." With this in mind, we must ask ourselves, "When a child affected by congenital Zika virus infection is in our waiting room, will we be sufficiently prepared to serve them? Will we even recognize them?"

Congenital Zika virus infection presents clear implications for practice in the field of Developmental-Behavioral Pediatrics. We suggest that providers conduct more comprehensive travel histories for both parents in both the preconception and the prenatal periods. While some children affected by Zika virus may have had prenatal ultrasounds documenting the findings presented here, some may not. It will therefore be important for providers to be alert for neurologic manifestations of Zika virus, other than microcephaly alone. We recognize that many of these manifestations may not yet be known. As a result, providers should make an effort to review the rapidly growing body of literature regarding congenital Zika virus, particularly as the first children affected by Zika grow older and complete developmental assessments. Providers should be aware of the social stigma associated with congenital Zika virus infection in parts of the world, like Brazil, and the added injury this can represent.[9] It is also important for providers to recall that environments characterized by stigma place children at risk for negative outcomes, including maltreatment and abandonment.

While children affected by congenital Zika virus infection will require multidisciplinary support, their families will require support as well. Specifically, they would be well-served by the patient- and family-centered medical home model, which includes care coordination, psychosocial family counseling, identification of community-based resources, and integrated primary care and specialist collaboration. With its roots in primary care and its expertise in developmental medicine, our field may be in the best position to lead such a model.

Each of us entered this field to make a difference in the lives of children with developmental concerns. Our specialty is dedicated to the principle that we should strive to help each child meet their full potential. We composed this document with these thoughts in mind, so that we can prepare, as a field, to best serve and meet the needs of children with congenital Zika virus infection.

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