

**SPECIAL REPORT**

## Zika Virus and Birth Defects — Reviewing the Evidence for Causality

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### SUMMARY

The Zika virus has spread rapidly in the Americas since its first identification in Brazil in early 2015. Prenatal Zika virus infection has been linked to adverse pregnancy and birth outcomes, most notably microcephaly and other serious brain anomalies. To determine whether Zika virus infection during pregnancy causes these adverse outcomes, we evaluated available data using criteria that have been proposed for the assessment of potential teratogens. On the basis of this review, we conclude that a causal relationship exists between prenatal Zika virus infection and microcephaly and other serious brain anomalies. Evidence that was used to support this causal relationship included Zika virus infection at times during prenatal development that were consistent with the defects observed; a specific, rare phenotype involving microcephaly and associated brain anomalies in fetuses or infants with presumed or confirmed congenital Zika virus infection; and data that strongly support biologic plausibility, including the identification of Zika virus in the brain tissue of affected fetuses and infants. Given the recognition of this causal relationship, we need to intensify our efforts toward the prevention of adverse outcomes caused by congenital Zika virus infection. However, many questions that are critical to our prevention efforts remain, including the spectrum of defects caused by prenatal Zika virus infection, the degree of relative and absolute risks of adverse outcomes among fetuses whose mothers were infected at different times during pregnancy, and factors that might affect a woman's risk of adverse pregnancy or birth outcomes. Addressing these questions will improve our ability to reduce the burden of the effects of Zika virus infection during pregnancy.