# Supplementary Online Content

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**eTable.** Case Definitions for Birth Defects Potentially Related to Zika Virus Infection During Pregnancy and Nationally Reported by Zika Pregnancy Registries and Monitored and Nationally Reported by Zika Birth Defects Surveillance

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable.** Case Definitions for Birth Defects Potentially Related to Zika Virus Infection During Pregnancy and Nationally Reported by Zika Pregnancy Registries and Monitored and Nationally Reported by Zika Birth Defects Surveillance

| Adverse Outcomes | Case Definitions | |
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| | **Zika Pregnancy Registries**<br>Pregnancies with laboratory evidence of possible Zika virus infection | **Active Birth Defects Surveillance[#]**<br>All birth defects potentially related to Zika virus infection during pregnancy (with codes noted for case-finding purposes)<br>Fetuses and infants with these birth defects should be monitored whether or not they had possible Zika virus exposure<br>Unless otherwise specified, the same defect descriptions and exclusion criteria for the Pregnancy Registries also apply to the Active Birth Defects Surveillance |
| **Laboratory evidence of possible Zika virus infection in pregnant woman, fetus, infant, or placenta[†]** | Required | Not required, but travel history and assessment of Zika virus exposure or symptoms including codes for arboviral disease noted in medical record should be abstracted |
| **Brain abnormalities with and without microcephaly** | | |
| *Confirmed or possible congenital microcephaly[¶]* | 1) Live births: measured head circumference (HC) adjusted for gestational age and sex <3rd percentile at birth[¶], or if not measured at birth, within first 2 weeks of life<br>2) Pregnancy loss: prenatal HC*,‡ more than 3 SD below the mean on prenatal ultrasound<br>OR<br>postnatal HC[¶] <3rd percentile | *Confirmed or possible congenital microcephaly[¶]*<br>1) Diagnosis of microcephaly or mention of microcephaly or small head in the medical record<br>**AND**<br>2a) Live births: measured head circumference (HC) adjusted for gestational age and sex <3rd percentile at birth[¶], or if not measured at birth, within first 2 weeks of life<br>OR<br>2b) Pregnancy loss: prenatal HC*,‡ more than 3 SD below the mean on prenatal ultrasound<br>OR<br>postnatal HC[¶] <3rd percentile<br>ICD-10-CM: Q02<br>CDC/BPA: 742.10, 742.486 |
| *Intracranial calcifications* | Intracranial (within the brain) calcifications, calcium deposits, or brightly echogenic foci<br>Seen on prenatal or postnatal cranial imaging‡ (ultrasound, CT, or MRI) | *Intracranial calcifications*<br>ICD-10-CM: No specific code; may be included under Q04.8, Q04.9<br>CDC/BPA: 742.48 |

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| *Cerebral / Cortical atrophy* | Atrophy or hypoplasia of cerebral structures<br>Seen on prenatal or postnatal cranial imaging‡ (ultrasound, CT, or MRI) | *Cerebral / Cortical atrophy*<br>ICD-10-CM: No specific code; may be included under Q04.3<br>CDC/BPA: 742.48 |
| *Abnormal cortical gyral patterns: Agyria, lissencephaly, microgyria, polymicrogyria, pachygyria, schizencephaly, gray matter heterotopia* | Pachygyria is a simplified and unusually thick gyral pattern and is considered a subset of lissencephaly by some. Microgyria and polymicrogyria are too many small folds in the cortical surface. Schizencephaly is the presence of abnormal clefts in the cerebral hemispheres. Gray matter heterotopia are clumps of gray matter located in the wrong place. Look for terms such as agyria, lissencephaly, microgyria, polymicrogyria, simplified gyral pattern, pachygyria, schizencephaly, heterotopia,cortical dysplasia, neuronal migration disorder<br>Seen on prenatal or postnatal cranial imaging‡ (ultrasound, CT, or MRI) | *Abnormal cortical gyral patterns: Agyria, lissencephaly, microgyria, polymicrogyria, pachygyria , schizencephaly, gray matter heterotopia*<br>ICD-10-CM: Q04.3, Q04.6, Q04.8<br>CDC/BPA: 742.24, 742.25, 742.28 |
| *Corpus callosum abnormalities* | Agenesis, hypoplasia, thin, partial, or absent corpus callosum<br>Seen on prenatal or postnatal cranial imaging‡ (ultrasound, CT, or MRI) | *Corpus callosum abnormalities*<br>ICD-10-CM: Q04.0<br>CDC/BPA: 742.21 |
| *Cerebellar abnormalities* | Atrophy or hypoplasia of the cerebellum or cerebellar vermis<br>Seen on prenatal or postnatal cranial imaging‡ (ultrasound, CT, or MRI) | *Cerebellar abnormalities*<br>ICD-10-CM: No specific code; may be included under Q04.3<br>CDC/BPA: 742.23, 742.31 |
| *Porencephaly* | Porencephaly describes a cavity or cyst within the cerebral hemisphere. Look for porencephaly or porencephalic cyst.<br>EXCLUDE: isolated choroid plexus cyst<br>Seen on prenatal or postnatal cranial imaging‡ (ultrasound, CT, or MRI) | *Porencephaly*<br>EXCLUDE: isolated choroid plexus cyst<br>ICD-10-CM: Q04.6<br>CDC/BPA: 742.41, 742.42 |
| *Hydranencephaly* | In hydranencephaly, all or part of the cerebral hemispheres are replaced by fluid-filled sacs. Look for hydranencephaly.<br>Seen on prenatal or postnatal cranial imaging‡ (ultrasound, CT, or MRI) | *Hydranencephaly*<br>ICD-10-CM: No specific code; should be included in Q04.3<br>CDC/BPA: 742.32 |

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| *Ventriculomegaly / Hydrocephaly* | Large, enlarged, or dilated cerebral ventricles (which may be specified as lateral, third or fourth ventricles), or hydrocephalus or ventriculomegaly<br>EXCLUDE: isolated "mild" ventriculomegaly without other brain abnormalities<br>Seen on prenatal or postnatal cranial imaging‡ (ultrasound, CT, or MRI) | *Ventriculomegaly / Hydrocephaly*<br>EXCLUDE: isolated "mild" ventriculomegaly without other brain abnormalities<br>ICD-10-CM: Q03.0–Q03.9<br>CDC/BPA: 742.30, 742.38, 742.39 |
| *Fetal brain disruption sequence* | Fetal brain disruption sequence components include: collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae | *Fetal brain disruption sequence*<br>No specific code. This might be coded as microcephaly or another single brain malformation, or all the components that might be coded individually.<br>ICD-10-CM: Q02, Q04.8, Q04.9<br>CDC/BPA: 742.10, 742.48<br>Include the following abnormalities only if co-existing abnormalities of the brain have been diagnosed:<br>ICD-10-CM: Q67.4, Q75.8, Q75.9, Q82.8<br>CDC/BPA: 754.08, 754.09, 756.08, 756.09, 757.39, 757.80 |
| *Other major brain abnormalities* | Any major brain abnormality not previously listed elsewhere including intraventricular hemorrhage (IVH) that clearly occurred in utero<br>Note: Exclude IVH acquired postnatally | *Other major brain abnormalities*<br>ICD-10-CM: Q04.0, Q04.3–Q04.9, Q07.00, Q07.02<br>CDC/BPA: 742.20, 742.22, 742.29, 742.48, 742.90 |
| **Neural tube defects (NTDs) and other early brain malformations** | | |
| *Anencephaly / Acrania* | Failure of the brain and skull to form.<br>Includes prenatal* or postnatal diagnosis of anencephaly | *Anencephaly / Acrania*<br>ICD-10-CM: Q00.0–Q00.2<br>CDC/BPA: 740.00-740.10, 740.20-740.29 |
| *Encephalocele* | Sac-like protrusion or projection of the brain and the membranes that cover it through an opening in the skull, resulting in an opening in the midline of the upper part of the skull, the area between the forehead and nose, or the back of the skull. | *Encephalocele*<br>ICD-10-CM: Q01.0–Q01.9<br>CDC/BPA: 742.00–742.09 |
| *Spina bifida* | An opening in the spine through which nerve tissue and/or meninges protrude. It can result in herniation of the brain into the foramen magnum (Arnold-Chiari malformation)<br>Prenatal or postnatal diagnosis of spina bifida or Arnold-Chiari malformation‡ | *Spina bifida*<br>ICD-10-CM: Q05.0–Q05.9, Q07.01, Q07.03<br>CDC/BPA: 741.00–741.99 |

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| *Holoprosencephaly / Arhinencephaly* | Failure of the forebrain to develop into two cerebral hemispheres, typically causing defects of the face and brain<br>Seen on prenatal or postnatal cranial imaging‡ (ultrasound, CT, or MRI) | *Holoprosencephaly / Arhinencephaly*<br>ICD-10-CM: Q04.1, Q04.2<br>CDC/BPA: 742.26, 742.27 |
| **Eye abnormalities** | | |
| *Microphthalmia / Anophthalmia* | Small or absent eye or eyes | *Microphthalmia / Anophthalmia*<br>ICD-10-CM: Q11.0–Q11.2<br>CDC/BPA: 743.00, 743.10 |
| *Coloboma* | A gap, notch or area of missing tissue in part of the eye, including the iris, choroid, lens, retina, or optic disc | *Coloboma*<br>ICD-10-CM: Q12.2, Q13.0, Q14.1–Q14.8<br>CDC/BPA: 743.34, 743.43, 743.48, 743.49, 743.51, 743.52, 743.535, 743.58, 743.59 |
| *Cataract* | Clouding of the lens of the eye diagnosed postnatally | *Cataract*<br>ICD-10-CM: Q12.0<br>CDC/BPA: 743.32 |
| *Intraocular calcifications* | Intraocular calcifications diagnosed postnatally | *Intraocular calcifications*<br>No specific code. This might be coded under the affected part of the eye.<br>ICD-10-CM: Q13.8, Q13.9, Q14.1–Q14.9<br>CDC/BPA: 743.48, 743.49, 743.51, 743.52, 743.58, 743.59 |
| *Chorioretinal anomalies involving the macula including chorioretinal atrophy and scarring, macular pallor, gross pigmentary mottling and retinal hemorrhage* | Changes in the posterior segment of the eye in particular involving the macula<br>EXCLUDE: retinopathy of prematurity | *Chorioretinal anomalies involving the macula including chorioretinal atropy and scarring, macular pallor, gross pigmentary mottling and retinal hemorrhage.* No specific code. This might be coded under the affected part of the eye.<br>ICD-10-CM: Q14.1–Q14.9<br>CDC/BPA: 743.51, 743.52, 743.53, 743.58, 743.59 |
| *Optic nerve atrophy, pallor, and other optic nerve abnormalities* | Optic nerve hypoplasia, optic nerve abnormalities, optic nerve pallor, double-ring sign, increased cup-to-disc ratio | *Optic nerve atrophy, pallor, and other optic nerve abnormalities*<br>ICD-10-CM: Q14.2, H47.03<br>CDC/BPA: 743.52 |

| **Consequences of central nervous system (CNS) dysfunction** | | |
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| *Congenital contractures and joint abnormalities (arthrogryposis, club foot with associated brain abnormalities, congenital hip dislocation with associated brain abnormalities)* | Arthrogryposis, joint contractures, decreased flexibility of the joints; talipes equinovarus or clubfoot with associated brain abnormalities; congenital hip dislocation or developmental dysplasia of the hip with associated with brain abnormalities | *Congenital contractures and joint abnormalities (arthrogryposis, club foot with associated brain abnormalities, congenital hip dislocation with associated brain abnormalities)*<br>Include all infants with arthrogryposis or multiple joint contractures.<br>Include talipes equinovarus or clubfoot only with associated brain abnormalities; Include congenital hip dislocation or developmental dysplasia of the hip only with associated brain abnormalities<br>ICD-10-CM: Q65.0–Q65.9, Q66.0–Q66.9, Q68.8, Q74.3<br>CDC/BPA: 754.30, 754.31, 754.50, 754.73 (excluding 754.735), 755.80 |
| *Congenital deafness* | Deafness documented by postnatal testing | *Congenital deafness*<br>ICD-10-CM: H90.0–H90.8, H90.A, H91.0-H91.9, Q16.0–Q16.9<br>CDC/BPA: 744.09 |

[#]ICD-10-CM codes included are for case-finding only. All potential diagnoses must be verified by record review and abstraction. CDC/BPA codes are listed for birth defects surveillance programs that use CDC/BPA codes for coding of birth defects (http://www.cdc.gov/ncbddd/birthdefects/documents/macdpcode0807.pdf).

[¶]Birth measurements based on intergrowth21 standards; http://intergrowth21.ndog.ox.ac.uk/Standard charts are based on measurements within 24 hours of birth, and therefore measurements within 24 hours of birth are appropriate for this assessment.

[†]Laboratory evidence of possible Zika virus infection in pregnant woman, fetus, infant, or placenta is defined as any of the following results on any clinical specimen (e.g., serum, urine, whole blood, cerebrospinal fluid, amniotic fluid, cord blood, saliva, placenta, umbilical cord tissue, placental membranes, or fetal tissue): Zika virus RNA detected by rRT-PCR; Zika virus IgM positive or equivocal AND Zika virus plaque reduction neutralization test (PRNT) titer ≥10 (regardless of dengue virus PRNT value); Zika virus IgM positive AND Zika virus PRNT not performed in following health department protocol; Zika virus IgM negative AND dengue virus IgM positive or equivocal AND Zika virus PRNT ≥10 (regardless of dengue virus PRNT value); culture of Zika virus; detection of Zika virus antigen.

*****Prenatal ultrasound measurements based on the Society for Maternal Fetal Medicine Standards, http://www.ajog.org/pb/assets/raw/Health%20Advance/journals/ymob/SMFM%20Statement_Fetal%20microcephaly.pdf

[‡]Prenatal findings should be confirmed by postnatal evaluation when possible. A suspected brain abnormality noted on prenatal evaluation that is clearly not present on postnatal evaluation should not be included.