



Congenital Zika Syndrome

Key Updates for Providers and Health System Managers

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Background

This brief summarizes current knowledge on congenital Zika syndrome (CZS), including estimated global burden, clinical characteristics, diagnosis, care, and follow-up recommendations for infants and affected families. As of January 4, 2018, the Pan American Health Organization (PAHO) reported 3,720 cases of confirmed CZS in the Americas, with the highest number of cases in Brazil (approximately 3,000), though substantial numbers of cases were also reported in Colombia, Guatemala, and the United States.¹ These numbers represent cases confirmed by laboratory tests and officially reported by ministries of health but do not include other suspected and possible cases. The true burden of CZS is likely higher than reflected in these numbers and has fallen on both families and health systems, requiring processes and resources to address the medical needs, disabilities, and social challenges that typically accompany CZS.



Photo Credit: Romilla Karnati

PAHO has put forth the following case definitions for CZS:²

Case definitions

Suspected case of congenital syndrome associated with Zika virus

- Live newborn who presents with:
 - Microcephaly: Head circumference below -2 standard deviations for gestational age and sex, measured at 24 hours postpartum according to the standardized reference, **OR**
 - Other congenital malformation of the central nervous system
- **AND** whose mother:
 - Traveled to or resided in an area where Zika virus vectors were present during her pregnancy, **OR**
 - Had unprotected sex during pregnancy with a partner who resided in or traveled to an area with the presence of Zika virus vectors.

Probable case of congenital syndrome associated with Zika virus

- Live newborn who meets the criteria for a suspected case of congenital syndrome associated with Zika virus, **AND**
- Who has intracranial morphological alterations detected by any imaging method and not explained by other known causes, **OR**
- Whose mother had rash during pregnancy

Confirmed case of congenital syndrome associated with Zika virus

- Live newborn who meets the criteria for a suspected case of congenital syndrome associated with Zika virus **AND** Zika virus infection was detected in specimens of the newborn, regardless of detection of other pathogens.

¹ Pan American Health Organization (PAHO). 2019. Zika Cumulative Cases. PAHO website.

https://www.paho.org/hq/index.php?option=com_content&view=article&id=12390:zika-cumulative-cases&Itemid=42090&lang=en.

² PAHO. 2016. *Guideline Zika Virus Disease and Complications Surveillance*. Washington, DC: PAHO.

Main characteristics of CZS

A range of congenital malformations has been associated with Zika infection during pregnancy. Recent literature supports that infections occurring earlier in pregnancy are more likely to be associated with severe manifestations of CZS. Currently, CZS is described by the following five features:³

- Severe microcephaly in which the skull has partially collapsed
- Decreased brain tissue with a specific pattern of brain damage, including subcortical calcifications
- Damage to the back of the eye, including macular scarring and focal pigmentary retinal mottling
- Congenital contractures, such as clubfoot or arthrogryposis
- Hypertonia that restricts body movement soon after birth

BOX 2. MEASURING HEAD CIRCUMFERENCE (12)

1. Anchor tape over eyebrows.
2. Pass tape over fullest part at the back of the head.
3. Check correct positioning.
4. Pull tight.
5. Record head circumference (cm) to last completed 1 mm.



Possible Damage to Central Nervous System with or without Microcephaly

A widely recognized consequence of CZS is microcephaly, defined as head circumference below -2 standard deviations for gestational age and sex, measured at 24 hours postpartum according to the standardized reference.⁴ Diagnosis of microcephaly requires attention to correct technique for head measurement.⁵

However, some cases of CZS do not present with microcephaly, and a normal head circumference may be due to hydrocephalus ex-vacuo (where unformed brain tissue is replaced by cerebrospinal fluid), so a head circumference that is normal or even large for gestational age does not change the diagnosis of CZS. Other findings, which may be aided by imaging techniques if available, may include intracranial calcifications, cerebral atrophy, abnormal cortical formation (polymicrogyria, lissencephaly, etc.), abnormalities of the corpus callosum, fetal brain disruption sequence (collapsed skull, prominent occiput, scalp folds), intraventricular hemorrhage, and neural tube defects (anencephaly, spina bifida).

Consequences of the dysfunction of the central nervous system

- As a result of the central nervous system malformations, other CZS manifestations include congenital contractures (e.g., clubfoot, arthrogryposis, and/or congenital hip dysplasia), congenital deafness, problems with swallowing, convulsions, and extreme irritability.

Ocular anomalies

- Macrophthalmia or anophthalmia, coloboma, cataracts, intraocular calcifications, macular anomalies (atrophy, scars, pallor), and optic nerve anomalies (atrophy, pallor) may occur.

Other possible consequences

- Infections with Zika virus during pregnancy can also result in placental infection and damage, severe growth restriction,

³ US Centers for Disease Control and Prevention (CDC). 2019. Congenital Zika Syndrome & Other Birth Defects. CDC website. <https://www.cdc.gov/pregnancy/zika/testing-follow-up/zika-syndrome-birth-defects.html>. [March 19, 2019.]

⁴ PAHO. 2019. Zika Resources: Case Definitions. PAHO website.

https://www.paho.org/hq/index.php?option=com_content&view=article&id=11117:zika-resources-case-definitions&Itemid=41532&lang=en.

⁵ CDC. 2016. "CDC's Response to Zika: Measuring Head Circumference." https://www.cdc.gov/zika/pdfs/microcephaly_measuring.pdf.

Initial evaluation of infants with suspected CZS

Infants born to women who may have been exposed to Zika virus infection in pregnancy require a thorough evaluation. Careful history taking can help to characterize the mother's history of Zika virus exposure, signs, and symptoms, including timing. Results of any maternal laboratory testing should be reviewed. The infant's head circumference needs to be measured and plotted in the relevant tables in the child's record of care within 24 hours of birth. Any other evident congenital abnormality should be noted. The following scenarios describe the recommended evaluation in each case⁶.

Infant with anomalies consistent with CZS and mother with laboratory evidence of infection

- Essential newborn care, including a complete physical examination
- Transfontanellar ultrasound and consider other neuroimaging methods (CT, MRI)
- Laboratory testing for Zika virus and for syphilis, toxoplasma, rubella, cytomegalovirus, and herpes simplex virus (STORCH)
- Ophthalmological and hearing tests
- Specialized consultations (neurology, physical therapy, etc.), if available
- Psychosocial support to the family

If the mother was not tested for Zika virus infection or tested when positive serology was no longer detectable, specific laboratory tests can be performed, including examination of the placenta, in settings with this capacity.

Infant with no anomalies consistent with CZS and mother with laboratory evidence of infection

- Essential newborn care, including a complete physical examination
- Transfontanellar ultrasound and consider other neuroimaging methods (CT, MRI), according to local capacity
- Laboratory testing for Zika virus, plus syphilis, toxoplasma, rubella, cytomegalovirus, and herpes simplex virus (STORCH)
- Ophthalmological and hearing tests

If the mother was not tested for Zika virus infection or was tested during the incorrect period of time, specific laboratory tests for her and her infant can be performed, including examination of the placenta, in settings with this capacity.

After the recommended evaluations, families of affected infants need to receive accurate and timely information on the diagnosis, management, and prognosis.

Follow-up⁷

Infants with confirmed or probable CZS need to receive follow-up at 2 weeks, 3 months, 6 months, 9 months, 12 months, 18 months, and 24 months at a minimum. Detailed assessment of growth, neurodevelopment, hearing, vision, and known complications (e.g., spasticity, seizures, or feeding problems) should be performed at each visit.

In children with no signs of CZS, routine monitoring of signs and symptoms that may appear later in infancy is recommended. Development should be closely monitored at minimum follow-up visits, as well as

⁶ World Health Organization (WHO). 2017. *WHO Toolkit: For the Care and Support of People Affected by Complications Associated with Zika Virus*. Geneva: WHO.

⁷ WHO. 2017. *WHO Toolkit: For the Care and Support of People Affected by Complications Associated with Zika Virus*. Geneva: WHO.

vision and hearing, including a physiological hearing test at least once before the age of 2 years. In case of deceleration of head growth or neurodevelopmental abnormalities with no identified etiology, it is recommended to restart investigation for Zika virus and re-evaluate the child at a referral health facility.

Management of CZS⁸

- Form a multidisciplinary care team with relevant specialists and community workers.
- Train caregivers, families, and community workers in promoting child development and providing support for daily functioning.
- Train caregivers and families to recognize potential complications, including seizures.
- Provide nutritional support for poor weight gain or feeding problems.
- Provide guidance for possible aspiration during feeding, including keeping the child upright during feeds and thickening food, if appropriate.
- Refer to an ophthalmologist if eye abnormalities are detected.
- Refer children with confirmed hearing impairment for appropriate hearing aids and speech therapy where available.
- Manage abnormal muscle tone with physical therapy, contractures with assistive devices, and spasticity with medication as necessary.
- Manage seizures with referral to pediatric neurology and an electroencephalogram, if possible.

Psychosocial support for families⁹

- Provide empathetic, supportive communication to families about the diagnosis and expected needs, including rehabilitation, close medical monitoring, developmental prognosis, and complications, such as potential feeding problems and seizures.
- Support caregivers and family members in stress management.
- If available, provide information on support groups and other resources.
- Refer caregivers and family members who show signs of severe distress to a mental health care provider.

Health System Considerations¹⁰

The recent Zika virus epidemic has revealed multiple health system gaps in affected countries, particularly with regard to availability and quality of specialty laboratory capacity, routine antenatal ultrasound, and diagnosis and management of congenital defects, including psychosocial support services for families of affected children. To prepare for future epidemics, pre-service education curricula (for nurses, doctors, child development professionals, and other relevant health providers), policy norms, and clinical protocols all need to be reviewed and updated; in-service training for the workforce needs to be planned, including services that support childhood development; basic equipment and supplies to support diagnosis and management of CZS need to be made available; surveillance and other methods for monitoring need to be strengthened; and communities and families need to receive timely and accurate information on how to take protective actions and receive adequate care.

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⁸ WHO. 2017. WHO Toolkit: *Toolkit: For the Care and Support of People Affected by Complications Associated with Zika Virus*. Geneva: WHO.

⁹ WHO. 2017. WHO Toolkit: *For the Care and Support of People Affected by Complications Associated with Zika Virus*. Geneva: WHO.

¹⁰ WHO. 2017. WHO Toolkit: *For the Care and Support of People Affected by Complications Associated with Zika Virus*. Geneva: WHO.