

Appendix 3.5

Case Inclusion Guidance for Potentially Zika-related Birth Defects

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Background

This document has been developed to provide guidance for reviewing and abstracting medical records of infants with defects potentially related to Zika virus. While it does not provide comprehensive information about each condition to be ascertained, it covers basic clinical descriptions, definitions of terms, and tips on how to look for and where to find information in the medical records.

Some of the conditions listed for ascertainment are not malformations themselves, but conditions that may result from the effects of Zika virus infection *in utero*. The intent is two-fold: 1) assist in identification of all infants potentially infected with Zika virus *in utero*, and 2) provide background information on the prevalence of these conditions regardless of the cause.

For programs that have never conducted population-based birth defects surveillance, the list of conditions for ascertainment will form the initial case definition for their activities. For programs that already conduct birth defect surveillance, the list of conditions may require a change in the case inclusion and/or case finding approach.

We hope this guide is helpful. Please contact Jan Cragan (jcragan@cdc.gov) or Cara Mai (cmai@cdc.gov) for questions or comments.

Brain Abnormalities with and without Microcephaly

Microcephaly

Description

Microcephaly, or microcephalus, is the clinical finding of a small head when compared with infants of the same sex and age. The head circumference (HC), also known as the occipitofrontal circumference (OFC), is considered a reliable assessment of the volume of the underlying brain. Microcephaly itself is not a malformation but a sign that the brain is abnormally small.



Inclusions

Congenital microcephaly – microcephaly that is present prenatally or at the time of birth/delivery.

For the purposes of surveillance for birth defects potentially linked to Zika, confirmed or possible congenital microcephaly is defined as:[¶]

- 1) Diagnosis of microcephaly or mention of microcephaly or small head in the medical record

AND EITHER 2a OR 2b:

- 2a) For Live Births: measured HC adjusted for gestational age and sex <3rd percentile at birth[¶]; or if not measured at birth, within first 2 weeks of life
- 2b) For Pregnancy Losses: prenatal HC*[‡] more than 3 standard deviations (SDs) below the mean on prenatal ultrasound; or postnatal HC[¶] <3rd percentile

[¶] HC percentiles for birth measurements should be based on the InterGrowth-21st standards. A tool for calculating percentiles for birth HC, weight, and length is available at:

<http://intergrowth21.ndog.ox.ac.uk/>. These standards are based on measurements within 24 hours of birth, and therefore measurements within 24 hours of birth are appropriate for this assessment.

*HC percentiles for prenatal ultrasound measurement should be based on the Society for Maternal Fetal Medicine standards. A table of fetal HC means and SDs by gestational age is available at:

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.

Exclusions

For the purpose of surveillance for birth defects potentially linked to Zika, the following should not be included:

- Children with a diagnosis or mention of microcephaly or small head in the medical record for whom the HC measurement is outside of the range mentioned above (see Inclusions)
- Children with a diagnosis or mention of microcephaly or small head in the medical record for whom no HC measurement is available. However, attempt should be made to ascertain the HC measurement at birth or within the first 2 weeks of life.
- Acquired microcephaly - Microcephaly that develops after birth due to a delivery complication or postnatal insult such as trauma or infection in infancy or childhood. In this instance, the head circumference (HC) is normal for sex and age at birth. However, the head becomes disproportionately smaller as the baby grows in length.

The diagnosis of microcephaly should not be assigned by surveillance staff based only on the HC value in the medical record. For the purpose of surveillance for birth defects potentially linked to Zika, there must be diagnosis or mention of microcephaly or small head in the medical record.

ICD-9-CM Codes 742.1 – Microcephalus

ICD-10-CM Codes Q02 – Microcephaly

CDC/BPA Codes 742.10 – Microcephalus
742.486 – Small brain

Diagnostic Methods Gold Standard – Head circumference measurement soon after delivery. Prenatal ultrasound or fetal MRI scan can estimate the HC during development. Microcephaly may be mentioned on head/brain ultrasound, CT or MRI scan, but not always. These procedures are not diagnostic.

Medical Records – what and where to look for information Mention of microcephaly on newborn physical exam (with HC measurement); results of prenatal ultrasound or fetal MRI scan; clinicians’ or nurses’ notes; results of postnatal head/brain ultrasound, CT or MRI scan

Associated Defects / Conditions Depending on the underlying cause of microcephaly, a variety of brain abnormalities may also be present. Brain abnormalities that have been described in children with potential Zika-associated microcephaly include intracranial calcifications (see page 5); hydranencephaly (see page 12);

polymicrogyria and other neuronal migration disorders (see page 7); agenesis of the corpus callosum (see page 8); cortical loss (see page 6); hydrocephalus *ex-vacuo* (see page 13); and fetal brain disruption sequence (see page 15).

Microcephaly also can result from the presence of other major congenital malformations such as spina bifida (see page 22) and holoprosencephaly (see page 24).

Prenatal Diagnoses Not Confirmed Postnatally Microcephaly can be detected on a mid-pregnancy anomaly scan (ultrasound) at 18-20 weeks. However, it may not be evident until the late 2nd or into the 3rd trimester. It is usually present by 36 weeks gestation. Serial prenatal ultrasounds may be needed to detect the development of microcephaly *in utero*. Prenatal findings should be confirmed by postnatal evaluation when possible.

Additional Information:

Some clinicians use other cut-points, such as less than the 5th or 10th percentile, to make a diagnosis of microcephaly. Microcephaly may also be mentioned in the medical record when the HC measurement is in the normal range for age and sex but small relative to the baby's weight and length. In other instances, microcephaly or a small head may not be mentioned in the medical record at all even though the measured HC is less than the 3rd percentile (or less than 3 SDs on prenatal ultrasound for a pregnancy loss). Surveillance programs may want to include infants with these conditions in their data. However, for the purposes of surveillance for birth defects potentially linked to Zika, only those infants or fetuses with mention of microcephaly or a small head in the medical record and a HC measurement that fits the stated criteria should be reported (see Inclusions).

The shape of the head after delivery can affect the accuracy of the HC measurement due to molding of the head from the birth canal.

Congenital microcephaly can result from: 1) an abnormality in the very early formation of the brain, often with a genetic etiology, or 2) arrest or destruction of normally-forming brain tissue, e.g, from infection or interruption of the blood supply during gestation. Although not all cases of microcephaly have an identifiable cause, known causes include:

- *In utero* infections such as cytomegalovirus (CMV), rubella, or *toxoplasmosis gondii*
- Chromosomal abnormalities, single gene disorders (syndromes), and mitochondrial mutations
- Teratogens including maternal alcohol use, certain medications, and toxins
- Maternal conditions such as poorly controlled diabetes, hyperphenylalaninemia, and severe malnutrition
- *In utero* ischemia or hypoxia (e.g., placental insufficiency or abruption)

Intracranial Calcifications

Description	Accumulations or deposits of calcium within the brain tissue. The calcifications themselves are not malformations but a sign of brain injury such as from infection, hemorrhage, or hypoxia (lack of oxygen).
Inclusions	Calcifications noted anywhere within the substance of the brain Brightly echogenic foci on ultrasound, CT or MRI scan
Exclusions	Calcifications associated with a brain tumor or thrombosis (blood clot) in a large blood vessel within the brain, such as might be seen with tuberous sclerosis or a transverse/straight sinus thrombosis
ICD-9-CM Codes	No specific code; may be included under 742.4 – Other specified anomalies of brain
ICD-10-CM Codes	No specific code; may be included under: Q04.8 – Other specified congenital malformations of brain Q04.9 – Congenital malformations of brain, unspecified
CDC/BPA Codes	742.48 – Other specified anomalies of brain
Diagnostic Methods	Gold standard – Prenatal or postnatal head/brain ultrasound, CT or MRI scan; autopsy or pathology Intracranial calcifications cannot be detected by physical exam.
Medical Records – what and where to look for information	Results of prenatal ultrasound or fetal MRI scan; consultation reports by neurologist, geneticist, infectious disease specialist, or other subspecialist; clinicians' or nurses' notes; results of postnatal head/brain CT or MRI scan; autopsy or pathology report
Associated Defects / Conditions	Depending on the underlying injury or cause of the calcification, a variety of brain abnormalities may also be present.
Prenatal Diagnoses Not Confirmed Postnatally	Intracranial calcifications may be included when only diagnosed prenatally on serial ultrasounds or a single fetal MRI scan. The certainty of the finding on a single prenatal ultrasound that does not persist on subsequent prenatal ultrasounds may be questionable. Prenatal findings should be confirmed by postnatal evaluation when possible.
Additional Information:	Some calcifications can be normal variants but usually in the context of an older person.

Causes of intracranial calcifications in a fetus or newborn include *in utero* infections such as cytomegalovirus (CMV), rubella, or *toxoplasmosis gondii*. In toxoplasmosis, the intracranial calcifications tend to be randomly distributed within the brain. In CMV, they tend to be distributed periventricularly (around the cerebral ventricles). The intracranial calcifications that have been described in children with birth defects potentially linked to Zika virus infection tend to be distributed in the region below the cerebral cortex (subcortical) and in other areas of the brain including the basal ganglia and brainstem. Other non-infectious causes include damage from anoxia (lack of oxygen) or intracranial hemorrhage (bleeding within the substance of the brain); vascular malformations within the brain, such as Sturge-Weber syndrome; storage diseases, such as Krabbe disease; and mitochondrial diseases.

Cerebral / Cortical Atrophy

Description	Atrophy is a general term which means the loss of cells, and hence the loss of size of the organ or tissue, usually after initial normal development. Cerebral, or cortical, atrophy refers to loss of cells within the two cerebral hemispheres, the main portion of the brain. It can affect all or part of one or both hemispheres. Cerebral atrophy itself is not a malformation but a sign of an underlying problem.
Inclusions	Atrophy of any part of the cerebral hemispheres Cerebral atrophy Cortical atrophy Cortical loss
Exclusions	Cerebral or cortical cysts Cerebral atrophy that is secondary to prematurity
ICD-9-CM Codes	No specific code; may be included under 742.2 – Reduction deformities of brain
ICD-10-CM Codes	No specific code; may be included under Q04.3 – Other reduction deformities of brain
CDC/BPA Codes	742.48 – Other specified anomalies of brain
Diagnostic Methods	Gold standard – Postnatal CT or MRI scan; autopsy or pathology Cerebral atrophy can also be described on prenatal or postnatal ultrasound. Cerebral atrophy cannot be diagnosed by physical exam, although associated neurologic symptoms may be noted.
Medical Records – what and where to look for information	Results of prenatal ultrasound or fetal MRI scan; consultation reports by neurologist, geneticist, or other subspecialist; clinicians’ or nurses’ notes; results of postnatal head/brain CT or MRI scan; autopsy or pathology report
Associated Defects / Conditions	Depending on the degree, cerebral atrophy can lead to reduced brain volume. As a result, the lateral ventricles are larger than normal (ventriculomegaly, see page 13). Likewise, there is often an increase in the cerebrospinal fluid between the brain and skull (extra-axial fluid). This is sometimes called “benign hydrocephalus”. Depending on the underlying condition that leads to cerebral atrophy, a variety of other brain abnormalities may also be present.
Prenatal Diagnosis	Cerebral atrophy may be included when only diagnosed prenatally on

**Not Confirmed
Postnatally**

serial ultrasounds.

The certainty of the finding on a single prenatal ultrasound that does not persist on subsequent prenatal ultrasounds may be questionable. Prenatal findings should be confirmed by postnatal evaluation when possible.

**Additional
Information:**

When the cerebral ventricles are enlarged for any reason, the surrounding cerebral tissue (cortex) can be compressed. This may give the erroneous appearance of cerebral atrophy on diagnostic ultrasounds or scans. It is important to carefully review all of the medical record to be certain of the diagnosis.

There are numerous events and disorders which can lead to cerebral atrophy, including fetal stroke, leukodystrophy and other inherited conditions, and congenital infections other than Zika.

Cerebral atrophy can also develop postnatally as a result of brain injury from postnatal intraventricular hemorrhage and other complications of prematurity. Cerebral atrophy that is related to prematurity should not be included in surveillance for birth defects potentially linked to Zika.

Abnormal Cortical Gyral Patterns

Description	The surface of the normal brain has convolutions (gyri) and groves (sulci), which look like folding of the brain. Changes in the pattern of the gyri and sulci reflect gross abnormalities in the structure of the cerebral (main portion of the brain) cortex. They may involve all or part of one or both cerebral hemispheres. There are several distinct and recognizable patterns of gyral abnormalities, and more than one abnormal pattern may be present in the same brain.
Inclusions	<p>Lissencephaly/Agyria –The terms mean “smooth brain.” The surface of the brain is smooth with no apparent gyri or only partially formed gyri.</p> <p>Pachygyria/Macrogyria/Incomplete lissencephaly– An area of the brain shows a reduced number of gyri which are wider than normal.</p> <p>Polymicrogyria – An area of the brain has an excessive number of small gyri.</p> <p>Gray matter heterotopia – The term heterotopia means “out of place.” It refers to neurons (brain cells) that have arrested (stopped) in their normal path of migration during brain development.</p> <p>Ectopia/Marginal glioneuronal heterotopias/Leptomeningeal heterotopias – Collections of neurons that have migrated beyond their normal limits during brain development.</p> <p>Neuronal migration disorder/Neuronal maturation disorder – Abnormal migration of neurons during brain development, which can lead to the various types of gyral malformations and heterotopia.</p> <p>Schizencephaly – Abnormal slits or clefts in the brain.</p> <p>Minor cortical dysplasias – Subtle disturbances in brain architecture that are more difficult to detect.</p>
Exclusions	Megalencephaly/Macrencephaly – The brain is abnormally large and heavy. It is thought to result from a disturbance in the regulation of the number of brain cells.
ICD-9-CM Codes	No specific code; may be included under: 742.2 – Reduction deformities of brain 742.4 – Other specified anomalies of brain
ICD-10-CM Codes	Q04.3 – Other reduction deformities of brain Q04.6 – Congenital cerebral cysts Q04.8 – Other specified congenital malformations of brain

CDC/BPA Codes	742.24 – Agyria and lissencephaly 742.25 – Microgyria 742.28 – Other specified reduction defect of brain
Diagnostic Methods	Gold standard: postnatal CT or MRI scan; autopsy or pathology. Abnormal gyral patterns may be suspected on prenatal ultrasound, fetal MRI scan, or postnatal head/brain ultrasound. They cannot be detected by physical exam.
Medical Records – what and where to look for information	Results of prenatal ultrasound or fetal MRI scan; consultation reports by neurologist, geneticist, or other subspecialist; clinicians’ or nurses’ notes; results of postnatal head/brain CT or MRI scan; autopsy or pathology report
Associated Defects / Conditions	A variety of other brain abnormalities may also be present.
Prenatal Diagnoses Not Confirmed Postnatally	Abnormal gyral patterns diagnosed by fetal MRI can be included. Gyral abnormalities suspected by prenatal ultrasound should be confirmed by postnatal evaluation for inclusion.

Additional Information:

During fetal development there are three steps to neuron (brain cell) development: first, the neurons develop and multiply; then they migrate to specific areas of the brain; and finally, they organize to form specific layers of the brain. Interference with any of these steps can result in abnormal migration and abnormal formation of the cerebral cortex. The clinical symptoms observed with these conditions depend on the extent of brain involvement and can range from profound developmental delay to mild dyslexia to none.

Abnormal gyral patterns have been described with fetal alcohol exposure and in a variety of genetic syndromes.

Corpus Callosum Abnormalities

Description	The corpus callosum is a broad band of nerve fibers in the central area of the brain that joins the two cerebral hemispheres. Most abnormalities reflect some degree of failure of development of the corpus callosum.
Inclusions	<p>Agenesis (absence) of the corpus callosum (ACC) – This can be either complete absence or partial absence.</p> <p>Hypoplasia (underdevelopment) of the corpus callosum</p> <p>Dysgenesis (defective development) of the corpus callosum</p> <p>Thinning of the corpus callosum</p>
Exclusions	--
ICD-9-CM	<p>No specific code; may be included under:</p> <p>742.2 – Reduction deformities of brain</p> <p>742.4 – Other specified anomalies of brain</p>
ICD-10-CM	Q04.0 – Congenital malformations of corpus callosum
CDC/BPA Codes	742.21 – Anomalies of corpus callosum
Diagnostic Methods	<p>Gold standard – Postnatal head/brain ultrasound, CT or MRI scan; autopsy or pathology</p> <p>Abnormalities of the corpus callosum may be suspected on prenatal ultrasound, fetal MRI scan, or postnatal head/brain ultrasound.</p> <p>Abnormalities of the corpus callosum cannot be detected by physical exam.</p>
Medical records –What and where to look for information	Results of prenatal ultrasound or fetal MRI scan; consultation reports by neurologist, geneticist, or other subspecialist; clinicians’ or nurses’ notes; results of postnatal head/brain ultrasound, CT or MRI scans; autopsy or pathology report
Associated defects/ Conditions	Corpus callosum abnormalities can be associated with a variety of other brain abnormalities, including microcephaly, macrocephaly, microgyria, pachygyria, or lissencephaly. Brain cysts in the area can block development of the corpus callosum. Abnormalities of the corpus callosum may also be seen with eye anomalies.
Prenatal Diagnoses Not Confirmed Postnatally	Abnormalities of the corpus callosum suspected prenatally should be confirmed by postnatal evaluation for inclusion.

Additional Information:

Abnormalities of the corpus callosum can result from congenital infections, chromosomal anomalies, fetal exposures such as alcohol, or blocked growth of the nerve fibers by brain cysts. They can occur in isolation, with other brain anomalies, or as part of a syndrome. Many people with isolated corpus callosum abnormalities appear to function normally and are diagnosed incidentally on procedures undertaken for other reasons.

Cerebellar abnormalities

Description	The cerebellum (“little brain”) is located at the back of the cerebral cortex (the main portion of the brain). It is divided into two hemispheres with a midline structure called the vermis. A variety of congenital abnormalities in its structure have been described.
Inclusions	<p>Cerebellar agenesis – Partial or complete absence of the cerebellum or any of its structures, the vermis, or hemispheres</p> <p>Cerebellar hypoplasia – Underdevelopment (decreased size) of the cerebellum or any of its structures, the vermis, or hemispheres</p> <p>Cerebellar dysplasia – Disorganized development of the cerebellar tissues. This can involve one area or the entire cerebellum</p> <p>Cerebellar atrophy – Decrease in size (due to loss of cells) after initial normal development of the cerebellum or any of its structures, the vermis, or hemispheres. This may be difficult to distinguish from hypoplasia if the process occurs early in development.</p> <p>Dandy Walker malformation – A constellation of abnormalities that includes hypoplasia of the cerebellar vermis, cystic enlargement of the 4th ventricle (the channel through which cerebrospinal fluid [CSF] flows from the brain to the spinal cord), and enlargement of the posterior fossa (base of the skull that contains the cerebellum). It results from narrowing, absence (atresia), or obstruction of the foramina of Magendie and Luschka (openings in the roof of the fourth ventricle) through which CSF normally flows out of the brain. The obstruction leads to hydrocephalus.</p> <p>Dandy Walker Blake continuum/Dandy Walker variant – These terms are sometimes used to denote the presence of a posterior fossa cyst and some degree of cerebellar dysgenesis. When encountering them, carefully review the medical record and abstract all of the specific cerebellar abnormalities described.</p> <p>Mega cisterna magna; large or prominent cisterna magna – Excessive prominence of the CSF space posterior to the cerebellum.</p> <p>Tectocerebellar dysraphia – Hypoplasia or aplasia of the cerebellar vermis with displacement of the cerebellar hemispheres</p> <p>Rhomboencephalsynapsis – Fusion of the two cerebellar hemispheres and absence of the vermis.</p> <p>Cerebellar cyst – A cyst described in any area of the cerebellum, the vermis, or hemispheres which is not part of any of the conditions described above.</p>
Exclusions	Chiari/Arnold-Chiari malformation – Herniation of part of the cerebellum through the foramen magnum into the spinal canal. There

are several types, one of which is often a complication of spina bifida. When present with associated spina bifida, code only as spina bifida. When present without associated spina bifida, code under Other major brain abnormalities (see page 18)

ICD-9-CM Codes

No specific code; may be included under:
742.2 – Reduction deformities of brain
742.4 – Other specified anomalies of brain

ICD-10-CM Codes

No specific code; may be included under Q04.3 – Other reduction deformities of brain

CDC/BPA Codes

742.23 – Anomalies of cerebellum
742.31 – Dandy-Walker syndrome

Diagnostic Methods

Gold standard – Postnatal CT or MRI scan; autopsy or pathology
Prenatal – Fetal MRI scan
Postnatal head/brain ultrasound (performed through the anterior fontanelle of the skull) cannot reliably evaluate the posterior fossa containing the cerebellum.
Cerebellar abnormalities cannot be diagnosed by physical exam, although associated neurologic symptoms may be noted.

**Medical Records –
what and where to
look for information**

Results of prenatal ultrasound or fetal MRI scan; consultation reports by neurologist, geneticist, or other subspecialist; clinicians' or nurses' notes; results of postnatal CT or MRI scans; autopsy or pathology report

**Associated Defects /
Conditions**

Hydrocephaly (see page 13).
A variety of other brain abnormalities may also be present, such as agenesis of the corpus callosum (see page 8).

**Prenatal Diagnoses
Not Confirmed
Postnatally**

Cerebellar abnormalities diagnosed by fetal MRI can be included. Cerebellar abnormalities suspected by prenatal ultrasound should be confirmed by postnatal evaluation for inclusion.

**Additional
Information:**

The cerebellum is one of the earliest structures of the brain to develop and its development one of the longest. Hence, the cerebellum is very vulnerable to developmental events.

Cerebellar anomalies are part of a number of genetic syndromes, including Joubert syndrome.

Porencephaly

Description	Porencephaly refers to cysts or cavities within the substance of the brain that become filled with cerebrospinal fluid (the fluid which surrounds the brain and spinal cord). The cysts are not malformations themselves but often a sign of brain injury. Examples of potential causes of such brain injury include infection, trauma, interruption of blood flow to the brain, or hypoxia (lack of oxygen).
Inclusions	Porencephaly Porencephalic cyst or cavity Encephaloclastic porencephaly Developmental porencephaly
Exclusions	Arachnoid cyst Cerebral cysts not described as porencephalic (see page 18) Choroid plexus cyst
ICD-9-CM Codes	742.4 – Other specified anomalies of brain
ICD-10-CM Codes	Q04.6 – Congenital cerebral cysts
CDC/BPA Codes	742.41 – Porencephaly 742.42 – Cerebral cysts
Diagnostic Methods	Gold standard – Postnatal CT or MRI scan; autopsy or pathology Prenatal ultrasound; fetal MRI scan; postnatal head/brain ultrasound Porencephaly cannot be detected by physical exam.
Medical Records – what and where to look for information	Results of prenatal ultrasound or fetal MRI scan; consultation reports by neurologist, geneticist, or other subspecialist; clinicians' or nurses' notes; postnatal head/brain ultrasound, CT or MRI scan; autopsy or pathology report
Associated Defects / Conditions	Porencephaly can be associated with a variety of other brain abnormalities, including microcephaly (see page 3) or macrocephaly (large head), microgyria (see page 7), absence of corpus callosum (see page 8), or absence of the septum pellucidum (a membrane separating the two cerebral hemispheres that is connected to the corpus callosum).
Prenatal Diagnoses Not Confirmed	Porencephaly diagnosed by fetal MRI can be included. Porencephaly suspected by prenatal ultrasound should be confirmed by postnatal

Postnatally evaluation for inclusion.

**Additional
Information:**

Porencephalic cysts can occur sporadically or can be familial or genetic. The severity of clinical symptoms varies greatly depending on the size and location of the porencephaly.

Hydranencephaly

Description	Hydranencephaly is a condition in which the brain’s cerebral hemispheres (the main portion of the brain) are replaced by cerebrospinal fluid (the fluid that surrounds the brain and spinal cord). The brain stem and cerebellum may be normal. Hydranencephaly is thought to result from a destructive process rather than a primary malformation, and may be an extreme form of porencephaly (see page 11).
Inclusions	Hydrancephaly – This can be either bilateral or unilateral
Exclusions	--
ICD-9-CM Codes	No specific code; may be included under: 742.3 - Congenital hydrocephalus 742.4 – Other specified anomalies of brain Note: For conditions coded under 742.3, it is important to distinguish severe hydrocephalus from true hydranencephaly through careful review of the medical record.
ICD-10-CM Codes	No specific code; should be included under Q04.3 – Other reduction deformities of brain
CDC/BPA Codes	742.32 - Hydranencephaly
Diagnostic Methods	Gold standard – Postnatal head/brain ultrasound, CT or MRI scan; autopsy or pathology. Can be noted on prenatal ultrasound or fetal MRI scan. Hydranencephaly cannot be diagnosed by physical exam, although associated neurologic symptoms may be noted.
Medical Records – what and where to look for information	Results of prenatal ultrasound or fetal MRI scan; consultation reports by neurologist, geneticist, or other subspecialist; clinicians’ or nurses’ notes; results of postnatal head/brain ultrasound, CT or MRI scans; autopsy or pathology report
Associated Defects / Conditions	--
Prenatal Diagnoses Not Confirmed Postnatally	Hydranencephaly may be included when only diagnosed prenatally. Prenatal findings should be confirmed by postnatal evaluation when possible.

**Additional
Information:**

Hydranencephaly may result from congenital infection or interruption of the blood supply to the brain that disrupts normal development.

Infants may appear normal at birth as the brainstem is intact. Head size is usually normal or maybe enlarged. After a few months, there are indications of developmental delay, increased muscle tone, and seizures. Few children with bilateral hydranencephaly survive past one year. Unilateral hydranencephaly has a much better prognosis with some children having only mild delays.

It is critical to distinguish true hydranencephaly from severe hydrocephalus (see page 13) through careful review of the medical record. In hydrocephalus when the cerebral ventricles are severely enlarged, the cerebral hemispheres may be so compressed as to appear nonexistent. This can be mistaken for hydranencephaly. Severe hydrocephalus can be treated with shunting of the CSF to allow expansion of the cerebral hemispheres. There is no treatment for hydranencephaly.

Ventriculomegaly/Hydrocephaly

Description

Ventriculomegaly refers to enlargement of the cerebral ventricles (the cavities within the brain that contain cerebrospinal fluid or CSF) as measured on diagnostic imaging (prenatal or postnatal ultrasound, CT or MRI scan).

Hydrocephaly, or hydrocephalus, refers to an increase in the amount of CSF within the cerebral ventricles, which enlarges their size and increases the pressure within the brain (intracranial pressure). It most commonly results from obstruction to the normal flow of CSF within the brain and spinal cord, but can also result from impaired absorption of CSF by brain tissue.

The distinction between ventriculomegaly and hydrocephalus has not been clearly defined, and these terms can be used interchangeably in medical records.

Inclusions

Aqueductal stenosis – Narrowing or obstruction of the aqueduct of Sylvius between the third and fourth ventricles. This is the most common type of obstructive hydrocephalus.

Occlusion of the foramina of Monro – Narrowing or obstruction of the channels that connect the lateral ventricles (the ventricles in the cerebral hemispheres) to the third ventricle in the midline.

Communicating hydrocephalus – Impaired absorption of CSF due to either 1) occlusion of the subarachnoid cisterns around the brainstem or 2) obliteration of the subarachnoid spaces around the exterior of the brain, leading to an increased amount of CSF within the brain.

Hydrocephaly due to other anatomic lesions such as agenesis of the corpus callosum, arachnoid and interhemispheric cysts, or Dandy-Walker malformation.

Hydrocephalus of unspecified type.

Ventriculomegaly that is described as moderate or severe.

Note: For an explanation of hydrocephalus *ex vacuo*, see Other Major Brain Abnormalities on page 18.

Exclusions	<p>For the purpose of surveillance for birth defects potentially linked to Zika, the following should not be included:</p> <ul style="list-style-type: none"> • Hydrocephalus diagnosed postnatally that results from a prior intracranial hemorrhage that occurred after delivery. In particular, this may be seen in preterm infants. • Hydrocephalus that occurs in association with spina bifida or encephalocele. Only the appropriate spina bifida or encephalocele code should be used. • Hydrocephaly that is associated with bone dysplasias such as achondroplasia (a form of dwarfism). <p>Colpocephaly – Enlargement of the posterior portion of the lateral ventricles resulting from abnormal development of the posterior part of the cerebral hemispheres.</p> <p>Ventriculomegaly that is described as mild.</p>
ICD-9-CM Codes	742.3 – Congenital hydrocephalus
ICD-10-CM Codes	<p>Q03.0 – Malformations of aqueduct of Sylvius</p> <p>Q03.1 – Atresia of foramina of Magendie and Luschka</p> <p>Q03.8 – Other congenital hydrocephalus</p> <p>Q03.9 – Congenital hydrocephalus, unspecified</p>
CDC/BPA Codes	<p>742.30 – Anomalies of aqueduct of Sylvius</p> <p>742.38 – Other specified hydrocephaly</p> <p>742.39 – Unspecified hydrocephaly</p>
Diagnostic Methods	<p>Gold standard – Postnatal head/brain ultrasound, CT or MRI scan; surgery; autopsy or pathology</p> <p>Hydrocephalus also can be seen on prenatal ultrasound or fetal MRI scan.</p> <p>Severe cases may be suspected by physical exam at delivery, but the diagnosis should be confirmed by postnatal imaging.</p>
Medical Records – what and where to look for information	Results of prenatal ultrasound or fetal MRI scan; consultation reports by neurologist, geneticist, or other subspecialist; clinicians' or nurses' notes (signs can include sunsetting eyes, tense fontanelle); results of postnatal head/brain ultrasound, CT or MRI scan; surgical notes; autopsy or pathology report
Associated Defects / Conditions	Hydrocephaly itself is not a malformation but a sign of an underlying condition causing increased CSF in the brain. A variety of other brain abnormalities may also be present, such as Chiari II malformation and neural tube defects (spina bifida and encephalocele).

Prenatal Diagnoses Severe cases may be included when only diagnosed prenatally.
Not Confirmed However, milder enlargement of the ventricles, when compared with
Postnatally prenatal reference values, may not be of clinical significance. Prenatal
findings should be confirmed by postnatal evaluation when possible,
and excluded if postnatal imaging studies are normal.

Additional Information

The ventricular system is made up of four ventricles connected by narrow passages – two lateral ventricles within the cerebral hemispheres, the third ventricle in the midline between the two lateral ventricles, and the fourth ventricle located within the brainstem and connected to the third ventricle. CSF normally flows through the ventricles and exits into cisterns that serve as reservoirs at the base of the brain. It bathes the surface of the brain and the spinal cord and is reabsorbed into the bloodstream.

Ventriculomegaly may be described as mild, moderate, or severe. How these designations correlate with the presence of true hydrocephalus, particularly when seen on prenatal ultrasound, has not been clearly defined.

While a child's head circumference may be increased for age in the presence of hydrocephaly, this measurement alone is not sufficient to make the diagnosis.

Hydrocephalus has a variety of etiologies, including infection, hemorrhage, and tumors as well as anatomic lesions of the brain such as agenesis of the corpus callosum, encephaloceles, cysts, and some bone dysplasias. In many cases, the etiology is not known.

It is critical to distinguish severe hydrocephaly from true hydranencephaly (see page 12) through careful review of the medical record. In hydrocephalus, when the cerebral ventricles are severely enlarged, the cerebral hemispheres may be so compressed as to appear nonexistent. This can be mistaken for hydranencephaly. Severe hydrocephalus can be treated with shunting of the CSF to allow expansion of the cerebral hemispheres. There is no treatment for hydranencephaly.

Fetal Brain Disruption Sequence

Description

Fetal brain disruption sequence is a pattern of congenital abnormalities that include severe microcephaly, overlapping cranial sutures, prominence of the occipital bone, and scalp rugae (excessive folding of the skin). These abnormalities are thought to result from partial disruption of the previously normal fetal brain during the 2nd or 3rd trimester of gestation which leads to significant decrease in intracranial pressure and collapse of the skull.



Inclusions

For inclusion, all components of the fetal brain disruption sequence (microcephaly, overlapping sutures, prominent occipital bone, scalp rugae) must be present.

Exclusions

Abnormally shaped head without associated microcephaly, overlapping sutures, or scalp rugae (e.g., asymmetric head/skull, brachycephaly, plagiocephaly, dolichocephaly, etc.).
 Overlapping cranial sutures without associated brain abnormalities or scalp rugae; do not code overlapping sutures if an isolated abnormality.
 Prominence or unusual shape of the occipital bone without associated brain abnormalities or scalp rugae; do not code prominence of the occipital bone if an isolated abnormality.

ICD-9-CM Codes

Case finding: There is no specific code for fetal brain disruption sequence. It might be coded as microcephaly or another single brain malformation, or all of the components might be coded individually.

- 742.1 – Microcephalus
- 742.4 – Other specified anomalies of brain
- 742.8 – Other specified anomalies of nervous system
- 742.9 – Other and unspecified malformations of brain

Defect coding: If fetal brain disruption sequence is present, code every component individually along with any additional brain or other abnormalities described.

Note: For the purpose of surveillance for birth defects potentially linked to Zika, do not include the following abnormalities if there are no coexisting abnormalities of the brain:

- 756.0 – Anomalies of skull and face bones
- 757.39 – Other specified anomalies of skin

ICD-10-CM Codes

Case finding: There is no specific code for fetal brain disruption sequence. It might be coded as microcephaly or another single brain malformation, or all of the components might be coded individually.

Q02 – Microcephaly

Q04.8 – Other specified congenital malformations of brain

Q04.9 – Congenital malformation of brain, unspecified

Defect coding: If fetal brain disruption sequence is present, code every component individually along with any additional brain or other abnormalities described.

Note: For the purpose of surveillance for birth defects potentially linked to Zika, do not include the following abnormalities if there are no coexisting abnormalities of the brain:

Q67.4 – Other congenital deformities of skull, face and jaw

Q75.8 – Other specified congenital malformations of skull and face bones

Q75.9 – Congenital malformation of skull and face bones, unspecified

Q82.8 – Other specified congenital malformations of skin

CDC/BPA Codes

Case finding: There is no specific code for fetal brain disruption sequence. It might be coded as microcephaly or another single brain malformation, or all of the components might be coded individually.

742.10 – Microcephalus

742.48 – Other specified anomalies of brain

Defect coding: If fetal brain disruption sequence is present, code every component individually along with any additional brain or other abnormalities described.

Note: For the purpose of surveillance for birth defects potentially linked to Zika, do not include the following abnormalities if there are no coexisting abnormalities of the brain:

fetal brain disruption sequence has not been diagnosed or described:

754.08 – Other specified deformity of skull

754.09 – Unspecified deformity of skull

756.08 – Other specified skull and face bone anomalies

756.09 – Unspecified skull and face bone anomalies

757.39 – Other specified anomalies of skin

757.80 – Other specified anomalies of skin

Diagnostic Methods

Gold standard – Definitive description of all components of the sequence (microcephaly, overlapping sutures, prominent occipital bone, scalp rugae) postnatally by physical exam, with or without confirmation by x-ray, CT or MRI scan. Look for mention of severe microcephaly, overlapping or overriding sutures/cranial bones, collapse of the skull, increased or redundant skin folds or rugae of the

scalp, and excessive scalp skin.
Collapse of the skull and associated brain abnormalities may be observed on prenatal ultrasound.

**Medical records –
what and where to
look for information**

Results of prenatal ultrasound or fetal MRI scan describing the skull and brain abnormalities; consultation reports by neurologist, geneticist, or other subspecialist; clinicians’ or nurses’ notes; head x-ray, CT or MRI scan; autopsy or pathology report

**Associated Defects /
Conditions**

Loss or destruction (partial or total) of cortical tissue in the brain
Paucity or absence of gyri
Hydranencephaly
Ventriculomegaly/Hydrocephalus
Alteration/disruption of the normal pattern of the cerebral ventricles
Absence of the thalamus and/or basal ganglia

**Prenatal Diagnoses
Not Confirmed
Postnatally**

These cases can be included when only diagnosed prenatally if there is specific description of the skull abnormalities indicating collapse with associated evidence of severe microcephaly or partial brain destruction. Excess folding of the scalp is sometimes seen on fetal MRI.

**Additional
Information:**

The occurrence of fetal brain disruption sequence has rarely been described with other congenital infections and is primarily seen with congenital Zika infection.

Intraventricular Hemorrhage that occurs *in utero*

Description	<p>Intraventricular hemorrhage (IVH) is bleeding inside or around the cerebral ventricles, the spaces within the brain that contain the cerebral spinal fluid. The bleeding can occur inside the ventricles only or can extend to the surrounding brain tissues. It can occur in small amounts or be extensive enough to enlarge the ventricles or compress the brain tissue. Bleeding in the brain can put pressure on the nerve cells and damage them. Severe damage to the nerve cells can lead to permanent brain injury.</p> <p>Bleeding from an IVH occurs most commonly in preterm infants during the first days after birth. This is postnatal IVH and is considered a complication of prematurity, not a congenital defect. However, bleeding from an IVH can occur <i>in utero</i> and can lead to enlargement of the ventricles and/or damage to the brain during gestation. Because this occurs prior to delivery, the resulting abnormalities are considered congenital for the purposes of reporting birth defects potentially linked to Zika.</p>
Inclusions	Any brain abnormalities that are described as related to <i>in utero</i> IVH. The specific abnormalities can vary depending on the timing during gestation and extent of the bleeding.
Exclusions	Postnatal IVH (when the bleeding occurs at some time after birth) is excluded. This is most common in preterm infants. If a postnatal IVH occurs in a full term infant, review the medical record closely to identify any qualifying brain abnormality that might have led to the IVH, but do not code the postnatal IVH itself.
ICD-9-CM Codes	<p>742.4 – Other specified anomalies of brain 742.9 – Unspecified anomaly of brain, spinal cord, and nervous system</p> <p>Note: These are the most likely codes for <i>in utero</i> IVH, but any of the individual brain abnormalities might be coded.</p>
ICD-10-CM Codes	<p>Q04.8 – Other specified congenital malformations of brain Q04.9 – Congenital malformation of brain, unspecified</p> <p>Note: These are the most likely codes for <i>in utero</i> IVH, but any of the individual brain abnormalities might be coded.</p>
CDC/BPA Codes	<p>742.48 – Other specified anomalies of brain 742.90 – Unspecified anomalies of brain</p> <p>Note: These are the most likely codes for <i>in utero</i> IVH, but any of the individual brain abnormalities might be coded.</p>

Diagnostic Methods	Gold standard – Postnatal head/brain ultrasound, CT, or MRI scan; autopsy or pathology Prenatal ultrasound or fetal MRI scan IVH cannot be diagnosed by physical exam.
Medical Records – what and where to look for information	Results of prenatal ultrasound or fetal MRI scan; consultation reports by neurologist, geneticist, or other subspecialist; clinicians’ or nurses’ notes; results of postnatal head ultrasound, CT, or MRI scan; autopsy or pathology report. Look for specific mention of an IVH that occurred or likely occurred <i>in utero</i> , during gestation, or before birth.
Associated Defects / Conditions	Ventriculomegaly Hydrocephalus Cerebral atrophy
Prenatal Diagnoses Not Confirmed Postnatally	<i>In utero</i> IVH may be included only when diagnosed prenatally. Prenatal findings should be confirmed by postnatal evaluation when possible.
Additional Information:	--

Other Major Brain Abnormalities

Description	Other congenital abnormalities of any part of the brain that are not included in other sections of this guide including, but not limited to, abnormalities of the thalamus, hypothalamus, pituitary, basal ganglia, and brainstem.
Inclusions	<p>Absence of the septum pellucidum</p> <p>Arnold-Chiari or Chiari malformation – Note: If associated with spina bifida, code only the spina bifida</p> <p>Septo-optic dysplasia</p> <p>Colpocephaly</p> <p>Cranial nerve defects</p> <p>Periventricular leukomalacia not due to prematurity</p> <p>Enlarged or truncated frontal horns</p> <p>Bilateral or multiple unilateral (all on the same side) subependymal cysts or pseudocysts</p> <p>Hydrocephalus <i>ex vacuo</i> – This is when the damaged brain shrinks and there is a resulting excess of CSF. However, the pressure within the brain is normal.</p> <p>Atrophy, aplasia, hypoplasia, or dysplasia of any part of the brain not included elsewhere</p> <p>Any congenital abnormality of any component of the brain not included elsewhere</p>
Exclusions	<p>Choroid plexus cyst</p> <p>Arachnoid cyst</p> <p>Isolated (single) subependymal cyst or pseudocyst</p> <p>Brain abnormalities included in other sections of this guide</p>
ICD-9-CM Codes	<p>742.2 – Reduction deformities of brain</p> <p>742.4 – Other specified anomalies of brain</p> <p>742.9 – Unspecified anomaly of brain, spinal cord, or nervous system</p>
ICD-10-CM Codes	<p>Q04.0, Q04.3–Q04.9 – Other congenital malformations of brain</p> <p>Q07.00, Q07.02 – Arnold-Chiari syndrome</p>
CDC/BPA Codes	Note: This list includes codes for brain anomalies that have not been specified in other defect categories. There may be conditions with codes specified in other categories that should be included under Other major brain abnormalities. All qualifying brain abnormalities not included in other defect categories should be included here regardless of the coding.

- 742.20 – Anomalies of cerebrum
- 742.22 – Anomalies of hypothalamus
- 742.29 – Unspecified reduction defect of brain
- 742.48 – Other specified anomalies of brain
- 742.90 – Unspecified anomalies of brain

Diagnostic Methods Gold standard – Postnatal head ultrasound, CT, or MRI scan; autopsy or pathology.
 Prenatal ultrasound or fetal MRI scan

Medical Records – what and where to look for information Results of prenatal ultrasound or fetal MRI scan; consultation reports by neurologist, geneticist, or other subspecialist; clinicians’ or nurses’ notes; results of postnatal head ultrasound, CT, or MRI scan; autopsy or pathology report. Look for mention of any abnormality of the cerebrum, cerebral hemispheres, cerebellum, thalamus, hypothalamus, corpus callosum, pituitary, basal ganglia, or brainstem.

Associated Defects / Conditions A variety of other brain abnormalities may also be present, including those in other sections of this guide.

Prenatal Diagnoses Not Confirmed Postnatally Many of these abnormalities may be described prenatally. Prenatal findings should be confirmed by postnatal evaluation when possible.

Additional Information:

This category is included in order to ascertain congenital brain abnormalities not specifically mentioned in the other defect categories.

Neural Tube Defects and Other Early Brain Malformations

Anencephaly/Acrania

Description

Anencephaly – Partial or complete absence of the brain and skull.
 Acrania – Absence of skull bones with some brain tissue present. These conditions may occur with or without co-occurring spina bifida.



Inclusions

Anencephaly
 Acrania
 Absent brain, with or without skull bones present.
 Craniorachischisis – Anencephaly continuous with an open posterior spinal defect with no meninges covering the nerve tissue (open spina bifida). Can be as limited as the cervical region or as extensive as the entire spine.
 Craniorachischisis with spinal retroflexion – Defect associated with severe flexion of the anterior portion of the spine.
 Exencephaly – Absence of the skull with some protruding brain tissue.
 Iniencephaly – A rare form of anencephaly where the head is bent severely backward, the neck is virtually absent, and the scalp is directly connected to the skin of the back.
 Holoanencephaly – Anencephaly that extends thorough the foramen magnum (involves the entire skull).
 Meroanencephaly – Defect limited to the anterior part of the brain and skull
 NOTE: The distinction between holoanencephaly and meroanencephaly is rarely made in the medical record.

Exclusions

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ICD-9-CM Codes

740.0 – Anencephalus
 740.1 – Craniorachischisis
 740.2 – Iniencephaly

ICD-10-CM Codes

Q00.0 – Anencephaly
 Q00.1 – Craniorachischisis

Q00.2 – Iniencephaly

CDC/BPA Codes

740.00 – Absence of brain
 740.01 – Acrania
 740.02 – Anencephaly
 740.03 – Hemianencephaly
 740.08 – Other anomalies similar to anencephaly
 740.10 – Craniorachischisis
 740.20 - 740.29 – Iniencephaly

Diagnostic Methods

Gold standard – Anencephaly is easily recognized on physical examination at delivery and autopsy or pathology

Medical Records – what and where to look for information

Results of prenatal ultrasound or fetal MRI scan; clinicians’ or nurses’ notes; physical exam; autopsy or pathology report. Look for a description of the infant/fetus after delivery.

Associated Defects / Conditions

Spina bifida that is not continuous with the anencephaly may also be present. Strings of tissue within the amniotic fluid surrounding the fetus may be noted on prenatal ultrasound or after delivery (amniotic band sequence).

Prenatal Diagnoses Not Confirmed Postnatally

Anencephaly may be included when only diagnosed prenatally. However, the prenatal findings should be confirmed by postnatal examination when possible.

Additional Information:

Anencephaly is one of a group of defects that result from failure of the neural tube to close (neural tube defects). In most instances, anencephaly is fatal within the first days or weeks after birth. Many cases can be prevented through consumption of folic acid before and during pregnancy. When present during gestation, strings of tissue within the amniotic fluid surrounding the fetus may interfere with growth and formation of the brain leading to anencephaly. This is called amniotic band sequence.

Maternal serum alphafetoprotein (MSAFP) and/or amniotic fluid alphafetoprotein (AFAFP) and amniotic fluid acetylcholinesterase (ACHE) may be elevated with anencephaly during pregnancy since the brain tissue is in contact with the amniotic fluid. However, these screening tests alone are not sufficient to diagnose the condition.

Encephalocele

Description Herniation of brain tissue and/or meninges (membranes covering the brain) through a defect in the skull. The hernia sac is usually covered by skin.



Inclusions Cephalocele
 Cranial meningocele – Herniation of meninges only.
 Encephalocele
 Encephalomyelocele - Herniation through a defect in a portion of both the skull and the upper spine.
 Encephalocystomeningocele
 Hydranencephalocele
 Meningoencephalocele
 Ventriculocele

Exclusions --

ICD-9-CM Codes 742.0 – Encephalocele

ICD-10-CM Codes Q01.0 - Q01.9 – Encephalocele

CDC/BPA Codes 742.00 - 742.09 – Encephalocele

Diagnostic Methods Gold standard – Postnatal head/brain ultrasound, CT or MRI scan; surgery; autopsy or pathology.
 Prenatal ultrasound or fetal MRI scan.
 Most cases of encephalocele are recognizable on physical examination after delivery but conclusively diagnosed only through imaging or direct visualization at surgery.

Medical Records – what and where to look for information Results of prenatal ultrasound or fetal MIR; physical exam after delivery; consultation reports by neurologist, geneticist, or other subspecialist; clinicians’ or nurses’ notes; results of postnatal head/brain ultrasound, CT or MRI scan; surgery notes; autopsy or pathology report

Associated Defects / Conditions Strings of tissue within the amniotic fluid surrounding the fetus may be noted on prenatal ultrasound or after delivery (amniotic band sequence).

**Prenatal Diagnoses
Not Confirmed
Postnatally**

Encephalocele may be included when only diagnosed prenatally. However, the prenatal findings should be confirmed by postnatal evaluation when possible. In addition, the absence of a small encephalocele on prenatal ultrasound does not necessarily mean that it will not be diagnosed after delivery.

**Additional
Information:**

Encephalocele is one of a group of defects that result from failure of the neural tube to close (neural tube defects). Some cases may be prevented through consumption of folic acid before and during pregnancy. When present during gestation, strings of tissue within the amniotic fluid surrounding the fetus may interfere with growth and formation of the brain leading to encephalocele. This is called amniotic band sequence. Occipital encephalocele is a component of Meckel-Gruber syndrome.

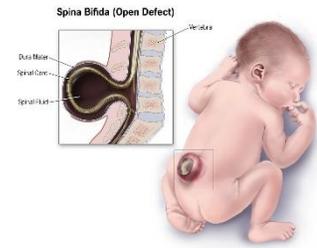
While encephaloceles that herniate through the visible exterior surface of the skull are most common, internal herniations through the sphenoid, maxillary, or ethmoid bones or the orbit or pharynx are also possible.

Maternal serum alphafetoprotein (MSAFP) and/or amniotic fluid alphafetoprotein (AFAFP) and amniotic fluid acetylcholinesterase (ACHE) usually are not elevated with encephalocele during pregnancy since the brain tissue is covered by skin and not in contact with the amniotic fluid. However, elevation of these screening tests does not necessarily rule out encephalocele.

Spina Bifida without Anencephaly

Description

Incomplete closure of the vertebral spine (usually posteriorly) through which spinal cord tissue and/or meninges (membranes that cover the spine) herniate.



Spina bifida may co-occur with anencephaly or acrania, either as a continuous or discontinuous defect.

Include these cases only under anencephaly/acrania (see page 19).

Inclusions

Any of the following defects in which anencephaly/acrania does not coexist:

- Lipomeningocele
- Lipomyelomeningocele
- Meningocele – Herniation of meninges only.
- Meningomyelocele, myelomeningocele – Herniation of both meninges and nerve/spinal cord tissue
- Myelocystocele
- Myelodysplasia
- Myeloschisis
- Open spina bifida – Spina bifida not covered by skin.
- Rachischisis – Open spina bifida without meninges covering the spinal cord tissue
- Spina bifida aperta
- Spina bifida cystica

Exclusions

- Closed spina bifida – Spina bifida that is covered by skin
- Diastematomyelia
- Diplomyelia
- Hydromyelia
- Spina bifida occulta – Incomplete closure of the spine without external herniation of meninges or spinal cord tissue. This usually is not visible exteriorly and may be asymptomatic.
- Syringomyelia (hydromyelia)
- Tethered spinal cord – Spinal cord tissue that is attached to one of the spinal vertebrae.

ICD-9-CM Codes

- Any of the following codes without an associated code in the range 740.0 – 740.2 (anencephaly/acrania, see page 19)
- 741.0 – Spina bifida with hydrocephalus
- 741.9 – Spina bifida without mention of hydrocephalus

ICD-10-CM Codes	Any of the following codes without an associated code in the range Q00.0 – Q00.2 (anencephaly/acrania, see page 19) Q05.0 - Q05.9 – Spina bifida with or without hydrocephalus Q07.01 – Arnold-Chiari syndrome with spina bifida Q07.03 – Arnold-Chiari syndrome with spina bifida and hydrocephalus
CDC/BPA Codes	Any of the following codes without an associated code in the range 740.00 – 740.29 (anencephaly/acrania, see page 19) 741.00 - 741.99 – Spina bifida with and without hydrocephalus
Diagnostic Methods	Gold standard – Physical exam; postnatal head/brain ultrasound, CT or MRI scan; surgery; autopsy or pathology Prenatal ultrasound or fetal MRI scan. Most instances of spina bifida result in a direct opening on the infant’s back that is easily recognized on physical examination after delivery. However, the exact nature of the defect (meningocele vs. myelomeningocele) may only be distinguished by CT or MRI scan, at surgery, or at autopsy.
Medical records – what and where to look for information	Results of prenatal ultrasound or fetal MRI; physical exam after delivery; consultation reports by neurologist, geneticist, or other subspecialist; clinicians’ or nurses’ notes; results of postnatal x-ray, head/brain ultrasound, CT or MRI scan; surgery notes, autopsy or pathology report
Associated Defects / Conditions	Ventriculomegaly (see page 13) Hydrocephalus (see page 13) Arnold-Chiari malformation (see page 18) Clubfoot (see page 34) Congenital hip dislocation, developmental dysplasia of the hip (see page 34) Strings of tissue within the amniotic fluid surrounding the fetus may be noted on prenatal ultrasound or after delivery (amniotic band sequence).
Prenatal Diagnoses Not Confirmed Postnatally	Spina bifida may be included when only diagnosed prenatally. However, the prenatal findings should be confirmed by postnatal evaluation when possible. In addition, the absence of spina bifida on prenatal ultrasound does not necessarily mean that it will not be diagnosed after delivery.
Additional Information:	

Spina bifida is one of a group of defects that result from failure of the neural tube to close (neural tube defects). Many cases may be prevented through consumption of folic acid before and during pregnancy. When present during gestation, strings of tissue within the amniotic fluid surrounding the fetus may interfere with growth and formation of the spine leading to spina bifida. This is called amniotic band sequence.

Spina bifida can occur at any level along the spinal column, from cervical (highest, at the neck) to thoracic, lumbar, and sacral (the lowest). When coding spina bifida, select the code for the highest level at which the spina bifida occurs. If the defect involves more than one level (e.g., cervicothoracic, thoracolumbar, lumbosacral), select the code for the highest level at which the spina bifida occurs. The highest level of involvement determines the degree of associated neurologic impairment.

Open spina bifida (spina bifida cystica, spina bifida aperta) are lesions that have no covering or are covered only by meninges (the membranes that cover the spinal cord). They usually leak cerebrospinal fluid (CSF). Closed lesions are covered by normal skin and do not leak CSF.

Hydrocephalus and Arnold-Chiari malformation of the brain frequently, though not always, result from spina bifida. When present, code only the spina bifida.

Maternal serum alphafetoprotein (MSAFP) and/or amniotic fluid alphafetoprotein (AFAFP) and amniotic fluid acetylcholinesterase (ACHE) may be elevated with anencephaly during pregnancy since the brain tissue is in contact with the amniotic fluid. However, these screening tests alone are not sufficient to diagnose the condition.

Maternal serum alphafetoprotein (MSAFP) and/or amniotic fluid alphafetoprotein (AFAFP) and amniotic fluid acetylcholinesterase (ACHE) may be elevated with spina bifida during pregnancy since the spinal cord tissue is in contact with the amniotic fluid. However, these screening tests alone are not sufficient to diagnose the condition.

Holoprosencephaly/Arhinencephaly

Description	Holoprosencephaly results from variable degrees of incomplete division of the brain into right and left cerebral hemispheres. There are four types which vary in severity: alobar, semi-lobar, lobar, and middle interhemispheric (MIHV). The condition can also affect development of the face and eyes. The most severely affected have one central eye (cyclopia) and a single tubular-shaped nose located above the eye (proboscis).
Inclusions	<p>Alobar holoprosencephaly – Complete lack of division of the cerebral hemispheres, resulting in one single ventricle instead of right and left lateral cerebral ventricles.</p> <p>Semi-lobar holoprosencephaly – Partial division of the cerebral hemispheres, with absence of the olfactory bulbs, absence of the corpus callosum, and underdeveloped (rudimentary) lobes of the cerebral hemispheres.</p> <p>Lobar holoprosencephaly – The cerebral hemispheres are mostly divided but remain fused in the front.</p> <p>Middle interhemispheric variant of holoprosencephaly (MIHV) – Lack of division of the posterior frontal and parietal lobes of the brain.</p> <p>Arhinencephaly – An older term for holoprosencephaly which refers more specifically to structural defects of the olfactory system or nose.</p> <p>Holotelencephaly – Holoprosencephaly with associated arhinencephaly</p> <p>Cyclopia – A form of holoprosencephaly where a single, central eye is present.</p> <p>Cebocephaly – A form of holoprosencephaly where the nose is underdeveloped (e.g., single nostril; proboscis) and closely set eyes (hypotelorism) are present.</p> <p>Ethmocephaly – A form of holoprosencephaly where the eyes are closely set (hypotelorism), the usual nose is absent, and a proboscis is present.</p>
Exclusions	Arhinencephaly without associated holoprosencephaly
ICD-9-CM Codes	742.2 – Reduction deformities of brain
ICD-10-CM Codes	Q04.1 – Arhinencephaly Q04.2 – Holoprosencephaly
CDC/BPA Codes	742.26 – Holoprosencephaly

742.27 – Arhinencephaly

Diagnostic Methods	Gold standard – Postnatal CT or MRI scan; autopsy or pathology Prenatal ultrasound or fetal MRI scan; postnatal head/brain ultrasound. Severe cases may be recognized on physical examination after delivery. However, the exact nature of the defect may only be distinguished by CT or MRI scan, or at autopsy.
Medical Records – what and where to look for information	Results of prenatal ultrasound or fetal MRI scan; physical exam after delivery; consultation reports by neurologist, geneticist, or other subspecialist; clinicians’ or nurses’ notes; results of postnatal head/brain ultrasound, CT or MRI scan; surgery notes, autopsy, or pathology report.
Associated Defects / Conditions	Associated facial features include cyclopia, proboscis, cebocephaly, ethmocephaly, cleft lip (usually midline), closely set eyes (hypotelorism), and/or absent or very small eyes (anophthalmia, microphthalmia, see page 26). Associated brain malformations include microcephaly (see page 3), hydrocephalus (see page 13), a single cerebral ventricle, and abnormal gyral patterns (agyria, microgyria, heterotopias, see page 7).
Prenatal Diagnoses Not Confirmed Postnatally	Holoprosencephaly may be included when only diagnosed prenatally. However, the certainty of the prenatal diagnosis may vary depending on the type and severity of holoprosencephaly. Prenatal findings should be confirmed by postnatal evaluation when possible.

Additional Information:

The different types of holoprosencephaly represent a continuum of anatomic severity. When possible, the specific type should be recorded. Alobar holoprosencephaly is commonly associated with facial anomalies that range from closely set eyes (hypotelorism) and median cleft lip (premaxillary agenesis) to cyclopia (a single central eye in the low frontal area) with absence of the usual nose and a proboscis (tubular-shaped nose located above the eye). Cebocephaly and ethmocephaly represent varying combinations of these facial anomalies.

Eye Abnormalities

Microphthalmia/Anophthalmia

Description	<p>Anophthalmia – Total absence of eye tissue or apparent absence of the globe of the eye in an otherwise normal orbit.</p> <p>Microphthalmia – Reduced volume of the eye. The corneal diameter is usually less than 10 millimeters, or the anteroposterior globe diameter is less than 20 millimeters.</p> <p>Anophthalmia or microphthalmia may affect one or both eyes, or there may be anophthalmia of one eye and microphthalmia of the other.</p>
Inclusions	<p>Anophthalmia</p> <p>Microphthalmia</p> <p>Nanophthalmia – Microphthalmia with normal internal eye (intraocular) structures. This is a distinct genetic condition.</p>
Exclusions	<p>“Small eyes” or “small palpebral fissures” for which the diagnosis of microphthalmia or anophthalmia has not been made.</p> <p>Microcornea with otherwise normal eye size.</p> <p>Cryptophthalmos – Failure of the eyelids to form. The eye is totally or partially covered with skin. However, if microphthalmia/anophthalmia or other qualifying eye abnormalities also are present, they should be included.</p>
ICD-9-CM Codes	<p>743.0 – Anophthalmos</p> <p>743.1 – Microphthalmos</p>
ICD-10-CM Codes	<p>Q11.0 – Cystic eyeball</p> <p>Q11.1 – Other anophthalmos</p> <p>Q11.2 – Microphthalmos</p>
CDC/BPA Codes	<p>743.00 – Anophthalmos</p> <p>743.10 – Microphthalmos</p>
Diagnostic Methods	<p>Gold standard – Physical examination after birth by an ophthalmologist; autopsy or pathology report</p> <p>These conditions also may be recognized after birth by a neonatologist, geneticist, or other clinician. However, the anteroposterior diameter of the globe can only be measured by postnatal ultrasound, CT or MRI scan, or autopsy.</p>

Medical Records – what and where to look for information	Clinicians' exam with close inspection of the eyes; consultation reports by ophthalmologist or geneticist; postnatal ultrasound of the head/brain/eye, CT or MRI scan with measurement of the anteroposterior diameter of the globe; autopsy or pathology report
Associated Defects / Conditions	Coloboma of the uvea, iris, choroid, and/or optic nerve (see page 27) Anophthalmia and microphthalmia can be associated with a variety of brain abnormalities.
Prenatal Diagnoses Not Confirmed Postnatally	Anophthalmia and microphthalmia may be suspected on prenatal ultrasound. However, they should not be included in surveillance data without postnatal confirmation. In addition, the absence of anophthalmia or microphthalmia on prenatal ultrasound does not necessarily mean that it will not be diagnosed after delivery.

**Additional
Information:**

Anophthalmia and microphthalmia are often accompanied by malformations of the brain and face, and frequently are components of genetic syndromes. Ophthalmologic examination of other family members, including the parents, for microphthalmia or blindness may be helpful in determining the cause.

Coloboma

Description	A coloboma is an abnormality of the eye where pieces of the eye structure are missing. A coloboma can be present in the iris (the colored part of the eye around the pupil), the lens (the clear structure behind the iris which focuses the light onto the retina), the retina (the light-sensitive tissue in the back of the eye), the choroid (the tissue layer behind the retina which contains the blood vessels), or the optic nerve which carries information from the eye to the brain. Colobomas can be found in one or both eyes.
Inclusions	Coloboma of any part of the eye, including the iris, lens, retina, choroid, optic nerve, or disc Ocular coloboma Uveoretinal coloboma
Exclusions	Coloboma of the eyelids
ICD-9-CM Codes	743.36 – Anomalies of lens shape 743.46 – Other specified anomalies of iris and ciliary body 743.47 – Specified anomalies of sclera 743.49 – Other coloboma and anomalies of anterior segment 743.52 – Fundus coloboma 743.56 – Other retinal changes, congenital 743.57 – Specified anomalies of optic disc 743.59 – Other congenital anomalies of posterior segment
ICD-10-CM Codes	Q12.2 – Coloboma of lens Q13.0 – Coloboma of iris Q14.1 - Q14.8 – Congenital malformations of posterior segment of eye
CDC/BPA Codes	743.34 – Coloboma of lens 743.43 – Coloboma of iris 743.48 – Other specified colobomas and anomalies of anterior segment 743.49 – Unspecified colobomas and anomalies of anterior segment 743.51 – Specified anomalies of retina 743.52 – Specified anomalies of optic disc 743.535 – Coloboma of choroid 743.58 – Other specified anomalies of posterior segment 743.59 – Unspecified anomalies of posterior segment
Diagnostic Methods	Gold standard - Physical examination, including a retinal exam, after

birth by an ophthalmologist; autopsy or pathology
 Colobomas of the iris can be apparent on physical exam after birth. The pupil appears keyhole-shaped rather than round. Colobomas of the lens and most posterior structures require examination with an ophthalmoscope.

**Medical Records –
 what and where to
 look for information**

Clinicians’ exam with close inspection of the eyes; consultation reports by ophthalmologist or geneticist; surgery reports, as examination of the eyes may be performed under anesthesia in young infants; autopsy or pathology report

**Associated Defects /
 Conditions**

Other eye anomalies also may be present, including cataracts (clouding of the lens of the eye), glaucoma (increased pressure inside the eye, also known as buphthalmos), and microphthalmos (see page 26).

**Prenatal Diagnoses
 Not Confirmed
 Postnatally**

Colobomas are unlikely to be diagnosed prenatally and should not be included if mentioned only on prenatal ultrasound without postnatal confirmation.

**Additional
 Information:**

During development, the eye begins as a bud and then folds in on itself leaving a small gap called the fetal cleft. This fetal cleft helps maintain the blood supply during eye development. At the final stage of development, the cleft closes from the back of the eye forward. A coloboma results when the cleft does not close properly.

Colobomas can be part of a genetic syndrome such as CHARGE.

Congenital Cataract

Description	A cataract is an opacity of the lens of the eye (the clear structure behind the iris which focuses light onto the retina in the back of the eye). Cataracts can affect any part of the lens, including the anterior, posterior, and zonular segments. Only cataracts that originate before birth should be included.
Inclusions	<ul style="list-style-type: none"> Infantile cataract Anterior polar cataract Lamellar cataract Nuclear cataract Posterior lentiglobus/lenticonus cataract Posterior cortical cataract Sectoral cataract Zonular cataract Cataract, type not specified
Exclusions	<p>Any of the above types of cataract that has its origin after birth.</p> <p>Opacities of the cornea (the clear transparent membrane covering the front of the eye over the iris)</p>
ICD-9-CM Codes	743.30 - 743.34 – Congenital cataract
ICD-10-CM Codes	Q12.0 – Congenital cataract
CDC/BPA Codes	743.32 – Cataract
Diagnostic Methods	<p>Gold standard - Physical examination after birth by an ophthalmologist; autopsy or pathology</p> <p>Some cataracts are readily apparent on physical examination. Others are only visible with an ophthalmoscope.</p>
Medical Records – what and where to look for information	<p>Clinicians' exam with close inspection of the eyes; consultation reports by ophthalmologist or geneticist; surgery reports, as examination of the eyes may be performed under anesthesia in young infants; autopsy or pathology report</p>
Associated Defects / Conditions	<p>Other eye anomalies also may be present, especially anomalies of the pupils including polycoria (more than one pupil in each eye) and ectopic (off-center) pupils, and anomalies of the lens. Anomalies of the head and central nervous system (brain and spinal cord) also may be present.</p>

**Prenatal Diagnoses
Not Confirmed
Postnatally**

Cataracts may be suspected by prenatal ultrasound, but should not be included in surveillance data without postnatal confirmation. In addition, the absence of a cataract on prenatal ultrasound does not necessarily mean that it will not be diagnosed after delivery.

**Additional
Information:**

Factors potentially contributing to congenital cataracts include congenital viral infections, chromosome anomalies, mutations in certain genes associated with cataracts, and a family history of eye defects.

Intraocular Calcification

Description	Abnormal deposits of calcium in the eye. These are not specific birth defects per se, but signs of injury.
Inclusions	Calcifications in any part of the eye, usually in the anterior segment. Brightly echogenic foci in the eye on ultrasound, CT or MRI scan.
Exclusions	--
ICD-9-CM Codes	No specific code. This might be coded under the affected part of the eye: 743.44 – Specified anomalies of anterior chamber, chamber angle, and related structures 743.48 – Multiple and combined anomalies of anterior segment 743.49 – Other coloboma and anomalies of anterior segment 743.54 – Congenital folds and cysts of posterior segment 743.55 – Congenital macular changes 743.56 – Other retinal changes, congenital 743.57 – Specified anomalies of optic disc 743.59 – Other congenital anomalies of posterior segment
ICD-10-CM Codes	No specific code. This might be coded under the affected part of the eye: Q13.8 – Other congenital malformations of anterior segment of eye Q13.9 – Congenital malformations of anterior segment of eye, unspecified Q14.1 - Q14.9 – Congenital malformations of posterior segment of eye
CDC/BPA Codes	No specific code. This might be coded under the affected part of the eye: 743.48 – Other specified colobomas and anomalies of anterior segment 743.49 – Unspecified colobomas and anomalies of anterior segment 743.51 – Specified anomalies of retina 743.52 – Specified anomalies of optic disc 743.58 – Other specified anomalies of posterior segment 743.59 – Unspecified anomalies of posterior segment
Diagnostic Methods	Gold standard - Physical examination, including retinal exam, after birth by an ophthalmologist; autopsy or pathology

Intraocular calcifications also might be seen on postnatal brain CT or MRI scan.

**Medical Records –
what and where to
look for information**

Consultation reports by ophthalmologist or geneticist; postnatal brain CT or MRI scan; surgery reports, as examination of the eyes may be performed under anesthesia in young infants; autopsy or pathology report
Look for mention of calcium deposits or calcification in any part of the eye.

**Associated Defects /
Conditions**

There may be associated abnormalities of the optic nerve, choroid or retina.
Intracranial calcifications within the brain can also be described on brain CT or MRI scan.

**Prenatal Diagnoses
Not Confirmed
Postnatally**

It is unlikely that these abnormalities would be detected by prenatal ultrasound, although they might be seen on a fetal MRI. However, they should not be included without postnatal confirmation.

**Additional
Information:**

Intraocular calcifications have been reported very rarely in infants with congenital Zika infection, but have not been well described.

Chorioretinal Atrophy, Scarring, Pigmentary Changes, Retinitis

Description	Changes in the retina (the light-sensitive tissue in the back of the eye) and/or the choroid (the tissue layer behind the retina which contains the blood vessels). The changes are not malformations themselves but a sign of injury from infection, bleeding, hypoxia (lack of oxygen), or other insults to structures in the back two-thirds of the eye.
Inclusions	Any abnormality of any part of the choroid, retina, or macula (area of the retina directly across from the pupil where vision is most perfect; its center is the known as the fovea), including but not limited to: <ul style="list-style-type: none"> – atrophy – hypoplasia – scarring – calcification – pigmentary mottling or clumping – hyperpigmentation – abnormal blood vessels – inflammation or infection
Exclusions	Retinopathy of prematurity
ICD-9-CM Codes	Note: No specific code. This might be coded under the affected part of the eye: 743.53 – Chorioretinal degeneration, congenital 743.54 – Congenital folds and cysts of posterior segment 743.55 – Congenital macular changes 743.56 – Other retinal changes, congenital 743.57 – Specified anomalies of optic disc 743.58 – Vascular anomalies of posterior segment 743.59 – Other congenital anomalies of posterior segment
ICD-10-CM Codes	Note: No specific code. This might be coded under the affected part of the eye: Q14.1 – Congenital malformation of retina Q14.2 – Congenital malformation of optic disc Q14.3 – Congenital malformation of choroid Q14.8 – Other congenital malformations of posterior segment of eye Q14.9 – Congenital malformation of posterior segment of eye, unspecified
CDC/BPA Codes	Note: No specific code. This might be coded under the affected part of the eye: 743.51 – Specified anomalies of retina 743.52 – Specified anomalies of optic disk 743.53 – Specified anomalies of choroid

743.58 – Other specific anomalies of posterior segment
 743.59 – Unspecified anomalies of posterior segment

Diagnostic Methods	Gold standard - Physical examination, including retinal exam, after birth by an ophthalmologist; autopsy or pathology
Medical Records – what and where to look for information	Consultation reports by ophthalmologist or geneticist; surgery reports, as examination of the eyes may be performed under anesthesia in young infants; autopsy or pathology report. Look for mention of abnormalities of the choroid and/or retina (chorioretinal), or macula (fovea).
Associated Defects / Conditions	There may be associated abnormalities, such as atrophy or hypoplasia, etc., of the optic nerve.
Prenatal Diagnoses Not Confirmed Postnatally	It is unlikely that these abnormalities would be detected by prenatal ultrasound. They should not be included without postnatal confirmation.

Additional Information:

The lining of the back two-thirds of the eye is composed of several layers (see illustration on page 41). The outer layer is the sclera, which is continuous with the cornea at the front of the eye. It is made up of a tough membrane that maintains the shape of the eye. The middle layer is the choroid, which is continuous with the ciliary body and iris at the front of the eye. The choroid is made up mostly of blood vessels with a layer of dark pigmentation. The inner layer is the retina, which is primarily made up by the nerves of the eye. The retina also contains a dark pigmented layer. It is the retina that receives the images of external objects. In the center of the retina posteriorly and directly across from the pupil (the opening in the iris), is an oval yellowish area called the macula. In its center is a depression called the fovea. It is here that the vision of external objects is most perfect.

Chorioretinal changes have been observed in congenital infections other than Zika, most notably toxoplasmosis and cytomegalovirus (CMV).

Optic Nerve Atrophy, Pallor, other Optic Nerve Abnormalities

Description	Abnormalities of the optic nerve that can be seen on eye examination where the optic nerve exits the retina at the back of the eye.
Inclusions	Any abnormality of the optic nerve, optic disc, or optic cup including but not limited to: <ul style="list-style-type: none"> - atrophy - hypoplasia - pallor (pale color) - increased optic cup to disc ratio - increased optic disc cupping
Exclusions	--
ICD-9-CM Codes	743.57 – Specified anomalies of optic disc
ICD-10-CM Codes	Q14.2 – Congenital malformation of optic disc H47.03 – Optic nerve hypoplasia
CDC/BPA Codes	743.52 – Specified anomalies of optic disc
Diagnostic Methods	Gold standard - Physical examination, including retinal exam, after birth by an ophthalmologist; autopsy or pathology
Medical Records – what and where to look for information	Consultation reports by ophthalmologist or geneticist; surgery reports, as examination of the eyes may be performed under anesthesia in young infants; autopsy or pathology report Look for mention of abnormalities of the optic nerve, optic disc, or optic cup.
Associated Defects / Conditions	There may be associated abnormalities, such as atrophy, hypoplasia, scarring, etc., of the choroid, retina, or macula (fovea).
Prenatal Diagnoses Not Confirmed Postnatally	It is unlikely that these abnormalities would be detected on prenatal ultrasound. They should not be included without postnatal confirmation.
Additional Information:	

The lining of the back two-thirds of the eye is composed of several layers. The innermost layer is the retina, which is made up mostly of the nerves of the eye. The optic disc is the area of the retina where the optic nerve exits the eye to the brain. It is at the back of the eye slightly to the nasal side of the macula (area of the retina directly across from the pupil where vision is most perfect). In the center of the optic disc is a white depression known as the optic cup. It usually measures about one-third or less of the diameter of the total optic disc.

Optic nerve abnormalities have been observed in congenital infections other than Zika, most notably toxoplasmosis and cytomegalovirus (CMV).

Consequences of Central Nervous System (CNS) Dysfunction

Arthrogryposis

Description	<p>Contracture (abnormal shortening and stiffness of the muscles, tendons, and/or ligaments) of the limbs that is present at birth. Arthrogryposis is not a single disease or diagnosis, but a characteristic appearance of the joints, which can vary from mild to severe. Most of the joints are flexed, but some can be extended. The contractures can be fixed or more flexible, and can involve all or most joints or a single joint. The surrounding muscles can be thin, absent (amyoplasia), or contain excess fibrous tissue (fibrotic).</p>
Inclusions	<p>Distal arthrogryposis – Involves just the hands and feet Arthrogryposis multiplex congenita (AMC) – Involves all joints Multiple pterygia – The contractures are accompanied by webbing of the skin across the affected joint(s) For the purpose of surveillance for birth defects potentially linked to Zika, include contracture of a single joint.</p>
Exclusions	<p>Posturing of the limbs in the flexed position due to increased muscle or nerve tone (hypertonia). Non-fixed, reducible positioning of the limbs or joints that can easily be moved to their typical neutral position.</p>
ICD-9-CM Codes	754.89 – Other specified nonteratogenic anomalies
ICD-10-CM Codes	<p>Q68.8 – Other specified congenital musculoskeletal deformities Q74.3 – Arthrogryposis multiplex congenita</p>
CDC/BPA Codes	755.80 – Arthrogryposis multiplex congenita
Diagnostic Methods	<p>Gold standard – Physical examination by a pediatric neurologist, geneticist, or orthopedic specialist. There is no single diagnostic test for arthrogryposis. Prenatal ultrasound of fetal limbs may suggest the diagnosis but is not considered diagnostic. Postnatal procedures that may assist in making the diagnosis include x-rays of the limbs (skeletal survey), muscle or skin biopsy, nerve testing (electromyogram or EMG, nerve conduction velocity or NCV), and CT or MRI scan of the brain; autopsy or pathology.</p>

**Medical Records –
What and where to
look for information** Results of prenatal ultrasound of the limbs or fetal MRI scan; consultation reports by neurologist, geneticist, orthopedist, or other specialists; clinicians' or nurses' notes; results of muscle or skin biopsy, nerve testing (electromyogram or EMG, nerve conduction velocity or NCV); results of postnatal CT or MRI scan of brain.; autopsy or pathology report

**Associated Defects /
Conditions** There may be associated brain or neurologic abnormalities.

**Prenatal Diagnoses
Not Confirmed
Postnatally** Arthrogryposis may be suggested on prenatal ultrasound of the limbs. Prenatal findings should be confirmed by postnatal evaluation when possible.

**Additional
Information:**

Because arthrogryposis is not a single disease or diagnosis, its identification in a newborn can lead to an extensive search for the underlying cause involving multiple subspecialists. Known factors that can contribute to arthrogryposis include lack of fetal movement *in utero* (fetal akinesia), which can have a variety of causes, chromosome abnormalities such as trisomy 18, and single gene disorders for which distal arthrogryposis is a component. The majority of people with the most common type of arthrogryposis have normal intelligence.

Clubfoot with associated brain abnormalities

Description

An abnormality of the foot consisting of plantar flexion (downward pointing of the foot and toes), inversion (internal rotation, or varus), and metatarsus adductus (deviation of the forefoot toward the body). An abnormally high arch (pes cavus) and midfoot flexion crease are also usually present, and the middle of the foot twists inward. A clubfoot usually cannot be returned to normal position and will interfere with normal walking if not corrected.



Clubfoot can occur alone or with other abnormalities as a consequence of neurologic impairment of the foot during development. For the purpose of surveillance for birth defects potentially linked to Zika, clubfoot should only be included if there are coexisting abnormalities of the brain.

Inclusions

Note: For the purpose of surveillance for birth defects potentially linked to Zika, include the following abnormalities only if there are coexisting abnormalities of the brain:
 Talipes equinovarus – Types include congenital, idiopathic, and neurogenic
 Talipes, not otherwise specified,
 Clubfoot, not otherwise specified.

Exclusions

Talipes equinovalgus
 Talipes calcaneovarus
 Talipes calcaneovalgus
 Talipes varus
 Talipes valgus
 Vertical talus
 Metatarsus adductus without the associated components of clubfoot
 Metatarsus varus without the associated components of clubfoot
 Pes varus
 Pes valgus
 Pes planus
 Rocker-bottom foot
 Positional or postural clubfoot

Note: For the purpose of surveillance for birth defects potentially linked to Zika, do not include the following abnormalities if there are no coexisting abnormalities of the brain:
 Talipes equinovarus – Types include congenital, idiopathic, and

ICD-9-CM Codes	neurogenic Talipes, not otherwise specified, Clubfoot, not otherwise specified. 754.51 – Talipes equinovarus 754.70 – Talipes, unspecified
ICD-10-CM Codes	Q66.0 - Q66.9 – Congenital deformities of feet
CDC/BPA Codes	754.50 – Talipes equinovarus 754.73 – Clubfoot, not otherwise specified (NOS), but exclude 754.735 – Congenital deformities of foot, NOS
Diagnostic Methods	Gold standard - Physical examination by an orthopedic specialist or geneticist; autopsy or pathology Clubfoot can be diagnosed by other clinicians. Prenatal ultrasound and postnatal X-rays of the foot may provide supplemental information but are not necessary for the diagnosis.
Medical Records – What and where to look for information	Results of prenatal ultrasound; consultation reports by orthopedics or genetics; clinicians’ and nurses’ notes; postnatal x-ray of the foot; results of surgical procedures; autopsy or pathology report
Associated Defects / Conditions	Clubfoot can also be associated with other musculoskeletal abnormalities such as torticollis (shortening of the neck muscle that tilts the head to one side) or developmental dysplasia of the hip (see page 36). It can also be a consequence of neurologic impairment of the foot during development.
Prenatal Diagnoses Not Confirmed Postnatally	Clubfoot can be identified or suspected on prenatal ultrasound. However, it should not be included without postnatal confirmation.

**Additional
Information:**

Clubfoot can occur on one foot or on both feet. The calf muscles on the affected side are usually permanently small. While in some instances the affected foot can be moved passively to a normal or near-normal position (so-called positional clubfoot), more commonly there is a component of rigidity, which can be severe.

Clubfoot often occurs alone, but can be associated with other musculoskeletal abnormalities such as torticollis (shortening of the neck muscle that tilts the head to one side) or developmental dysplasia of the hip (see page 36) and with genetic syndromes such as triploidy, Larsen syndrome, or Moebius sequence. Neurogenic clubfoot results from neurologic impairment of the foot during development due to conditions such as spina bifida, arthrogryposis, sacral agenesis, spinal muscular atrophy, and others that cause paralysis.

The terminology describing foot deformities can be confusing. The term “clubfoot” is often used in the medical record to mean talipes equinovarus, but it can also be used to refer to other conditions such as metatarsus adductus or talipes calcaneovarus. Terms used in describing foot deformities include:

talus – ankle

pes – foot

talipes – ankle/foot

equino – heel elevated (like a horse)

varus – turned inward

valgus – turned outward

dorsi flex – flexed upward

plantar flex – flexed downward

adductis – toward midline

abductis – away from midline

Congenital Hip Dislocation / Developmental Dysplasia of the Hip with associated brain abnormalities

Description	<p>Congenital hip dislocation (also known as developmental dysplasia of the hip or DDH) occurs when the head of the femur (bone of the upper leg) is located outside its normal position in the cup-shaped cavity formed by the hip bone (acetabulum). In some instances, the femur can be passively placed back into position; in others, physical treatment with surgery is required. The depth and shape of the acetabulum can also be abnormal.</p> <p>Congenital hip dislocation can occur alone or with other abnormalities as a consequence of neurologic impairment during development. For the purpose of surveillance for birth defects potentially linked to Zika, congenital hip dislocation should only be included if there are coexisting abnormalities of the brain.</p>
Inclusions	<p>Note: For the purpose of surveillance for birth defects potentially linked to Zika, include the following abnormalities only if there are coexisting abnormalities of the brain:</p> <ul style="list-style-type: none"> Congenital hip dislocation Developmental dysplasia of the hip (DDH) Teratologic hip dislocation
Exclusions	<ul style="list-style-type: none"> Flexion deformity or contracture of the hip Hip click Predislocation of the hip Preluxation of the hip Subluxation of the hip Unstable hip <p>Note: For the purpose of surveillance for birth defects potentially linked to Zika, do not include the following abnormalities if there are no coexisting abnormalities of the brain:</p> <ul style="list-style-type: none"> Congenital hip dislocation Developmental dysplasia of the hip (DDH) Teratologic hip dislocation
ICD-9-CM Codes	<ul style="list-style-type: none"> 754.30 – Congenital dislocation of hip, unilateral 754.31 – Congenital dislocation of hip, bilateral 754.35 – Congenital dislocation of one hip with subluxation of other hip
ICD-10-CM Codes	<ul style="list-style-type: none"> Q65.0 - Q65.9 – Congenital deformities of hip

CDC/BPA Codes	754.30 – Congenital dislocation of hip 754.31 – Unstable hip
Diagnostic Methods	Gold standard – Postnatal ultrasound of the hip Hip dislocation may be suspected on prenatal ultrasound and is sometimes diagnosed by physical examination or postnatal x-ray of the hip.
Medical Record – What and where to look For information	Results of prenatal ultrasound; physical examination of the hip after delivery; consultation reports by orthopedics or genetics; clinicians’ and nurses’ notes; postnatal ultrasound or x-ray of the foot; results of surgical procedures; autopsy or pathology report
Associated Defects/ Conditions	Congenital hip dislocation can be associated with other musculoskeletal abnormalities such as torticollis (shortening of the neck muscle that tilts the head to one side) or clubfoot (see page 34). It also can be a consequence of neurologic impairment during development.
Prenatal Diagnoses Not Confirmed Postnatally	While this condition may be suspected by prenatal ultrasound, it should not be included in surveillance data without postnatal confirmation. In addition, the absence of hip dislocation on prenatal ultrasound does not necessarily mean that it will not be diagnosed after delivery.

Additional Information:

The hip on either side alone can be dislocated, or both hips can be dislocated. The terminology describing congenital hip dislocation has changed over time, and congenital hip dislocation is now more often referred to as hip dysplasia or developmental dysplasia of the hip (DDH). An unstable hip, in which the femoral head may be moved in and out of the acetabulum on physical examination of the newborn, often resolves spontaneously over time in young infants. However, a truly dislocated hip in which the femoral head remains out of the acetabulum for a prolonged period may result in acetabular deformity unless treated. In some instances, the hip joint is already abnormal (dysplastic) at the time of birth, which can result in hip dislocation. Hence, the designation developmental dysplasia of the hip.

The stability of the hip joint may be evaluated on physical examination using the Barlow test or Ortolani maneuver. Pressure is applied to the hip with the knees flexed to attempt to move the head of the femur out of the hip joint or to move it back into normal position in the acetabulum. The presence of either sign indicates a hip dislocation is present. However, the absence of these signs does not necessarily mean that a dislocation is not present. In some instances, the femoral head may be fixed in a dislocated position and cannot be moved in or out of the joint.

Congenital hip dislocation occurs more frequently after footling or breech deliveries and is more common in females than males. It is most often an isolated condition, although it may occur with

generalized skeletal abnormalities and in some genetic syndromes. It can be part of the caudal regression sequence. Some instances of congenital hip dislocation are probably familial.

Congenital Hearing Loss (unilateral or bilateral)

Description	Loss of hearing in one or both ears present at birth or loss that may develop later but is due to infection, genetic causes, or other influences that affected the fetus while <i>in utero</i> . Hearing loss can be of two basic types: 1) Sensorineural - Hearing loss that occurs when there is a problem in the way the inner ear or nerve works; 2) Conductive hearing loss - Hearing loss caused by something that stops sounds from getting through the outer or middle ear. Hearing loss can also be of mixed type with both sensorineural and conductive components. It can also result from damage to the inner ear or nerve that results in failure of sound to be organized in a way that the brain can understand (auditory neuropathy).
Inclusions	<ul style="list-style-type: none"> Sensorineural hearing loss Sensory hearing loss Neural hearing loss Permanent conductive hearing loss Mixed hearing loss (mixed conductive and sensory hearing loss) Auditory neuropathy Auditory neuropathy spectrum disorder Auditory dyssynchrony Central hearing loss External auditory canal atresia Aural atresia
Exclusions	Transient conductive hearing loss
ICD-9-CM Codes	<ul style="list-style-type: none"> 389.0 - 389.9 – Hearing loss 744.00 - 744.09 – Anomalies of ear causing impairment of hearing 794.15 Abnormal Auditory Function Studies
ICD-10-CM Codes	<ul style="list-style-type: none"> H90.0 - H90.8 and H90.A – Conductive and sensorineural hearing loss H91.0 - H91.9 – Other and unspecified hearing loss Q16.0 - Q16.9 – Congenital malformations of ear causing impairment of hearing
CDC/BPA Codes	<ul style="list-style-type: none"> 744.09 – Unspecified anomalies of ear with hearing impairment <p>Note: The CDC/BPA code does not include hearing loss not associated</p>

with an ear anomaly

Diagnostic Methods

Gold standard: Auditory Evoked Potentials (also known as Auditory Brainstem Response or ABR) using frequency-specific stimuli and including air and bone conduction thresholds to determine peripheral hearing levels in infants less than 4-6 months.

Visual Reinforcement Audiometry (VRA) is recommended for behavioral evaluation in children from 4-6 months (corrected for gestational age if preterm) until approximately 24 months. This includes audiologic assessment for ear specific tones and speech stimuli along with Otoacoustic Emissions (OAE) testing and tympanometry or potentially acoustic reflex thresholds. ABR should be performed if the behavioral audiologic evaluation yields conflicting or inconsistent results.

**Medical Records –
what and where to look
for information**

Often diagnosis is completed in an outpatient setting. Look for consultation reports by audiology, otolaryngology (ENT), genetics, or craniofacial specialist/team; results of postnatal CT or MRI scan of the ear and brain.

**Associated Defects /
Conditions**

Craniofacial anomalies
Microtia (small abnormally-shaped ear).
Absence/atresia of the external auditory (ear)
canal Absence/atresia of the ear

**Prenatal Diagnoses Not
Confirmed Postnatally**

Hearing loss cannot be diagnosed prenatally.

**Additional
Information:**

For the purposes of surveillance for birth defects potentially linked to Zika, it is suggested that ascertainment be limited to congenital hearing loss in infants one year of age or younger.

All infants receive hearing screening soon after birth. This is usually done at the birth hospital before the newborn is discharged, but sometimes may be done later. A failed hearing screen does not diagnose hearing loss, but requires follow up evaluation, which is usually done on an out-patient basis. Verifying a diagnosis of hearing loss may require review of out-patient physician’s and/or audiologist’s records.

Because ABR is not a test of hearing itself but rather a measure of electrophysiologic response to

auditory stimulation, confirmation of hearing perception requires behavioral evaluation as soon as the child is developmentally capable of providing reliable and valid behavioral responses to sound.

Most hearing loss associated with congenital Zika infection is assumed to be sensorineural. Diagnostic ABR is more indicative of possible hearing loss in these children. Results of automated ABR screening and OAE screening or non-ear-specific soundfield studies are not sufficient for a diagnosis of hearing loss. While hearing loss related to congenital Zika infection may be evident on testing at birth, the onset of hearing loss might be delayed or progressive over time in some infants.

A CT or MRI scan of the ear and brain can identify an abnormally formed cochlea, absent or reduced auditory nerve volume (cranial nerve VIII), or malformed or absent auditory cortex or temporal lobe. These would indicate the presence of permanent end organ hearing loss or a disorder of auditory processing. Hearing loss may be part of many genetic syndromes with DNA mutations in genes known to cause hearing loss (e.g., *Connexin 26*). Prenatal genetic testing potentially could reveal a syndrome that is known to include hearing loss as one of the sequelae.

Figure 1. Brain – Exterior View

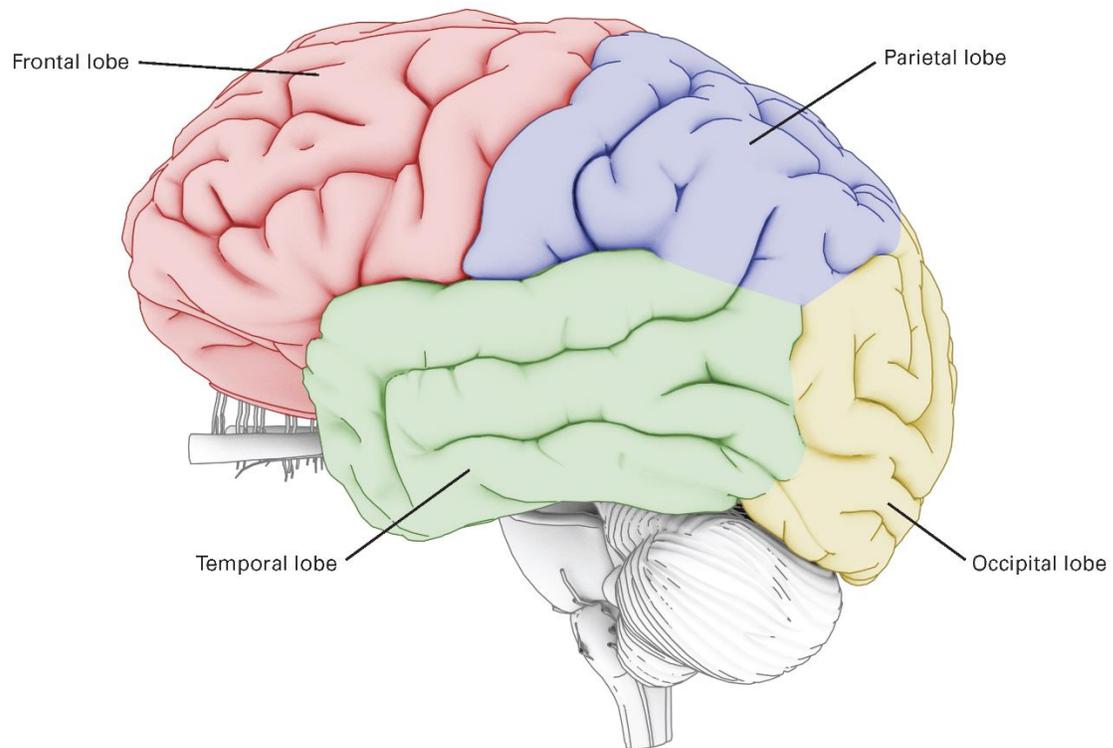


Figure 2. Brain - Cross-section View

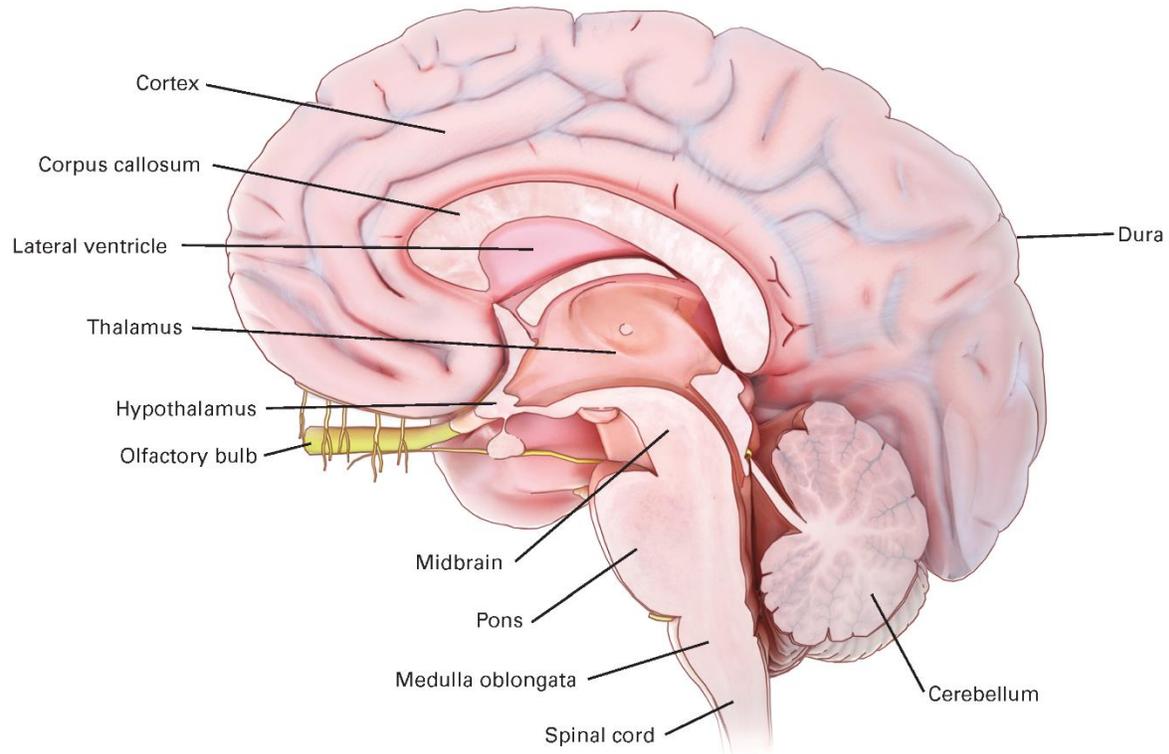


Figure 3. Skull – Exterior View

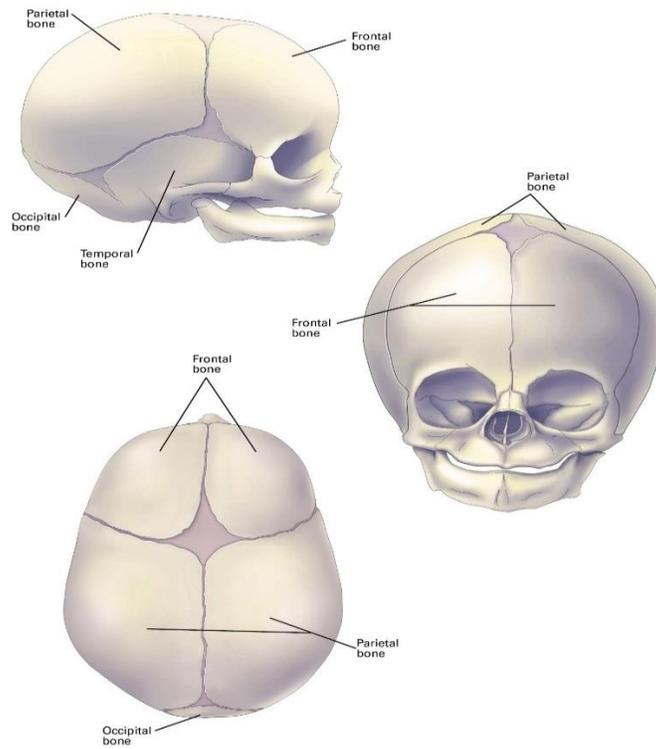
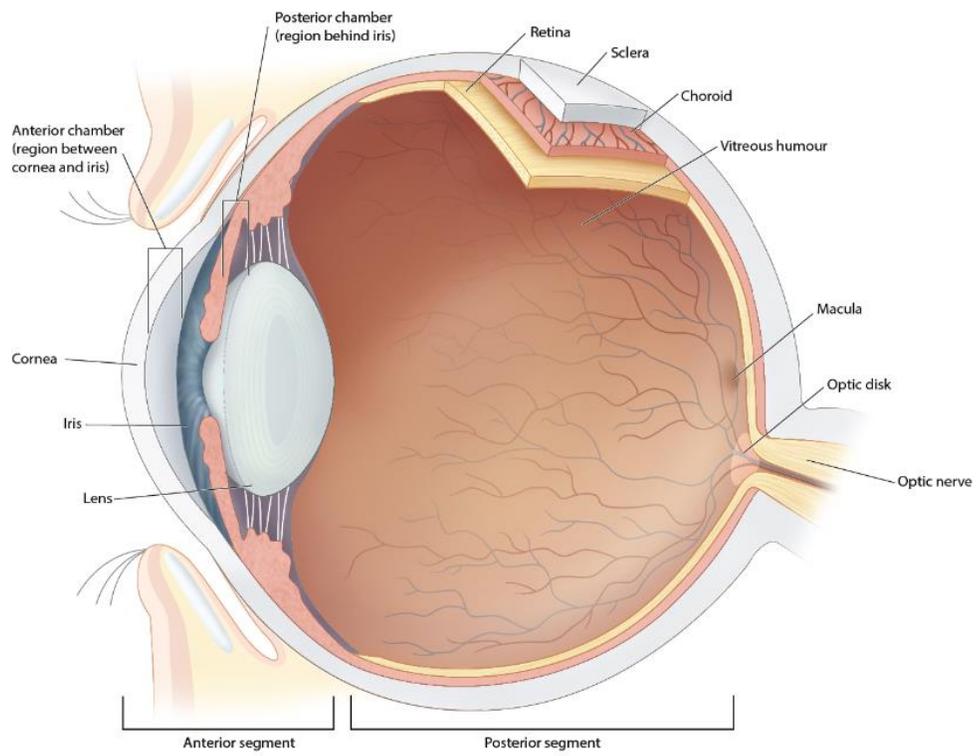


Figure 4. Eye – Cross-section View



Glossary of Terms¹⁻⁵

General Terminology

Major anomaly - A congenital abnormality that requires medical or surgical treatment, has a serious adverse effect on health and development, or has significant cosmetic impact. Individual major anomalies occur in less than 1% of the population. Together, they are seen in approximately 3% of births. Examples include cleft lip and tracheo-esophageal fistula.

Minor anomaly - A congenital abnormality that does not require medical or surgical treatment, does not seriously affect health and development, and does not have significant cosmetic impact. Individual minor anomalies generally occur in less than 4% of the population. The presence of multiple minor anomalies in the same child may provide clues to the timing of a prenatal insult and may indicate the presence of an undiagnosed major anomaly, syndrome, or functional deficit. Examples of minor anomalies are listed in Appendix B.

Normal variant - A minor anomaly that occurs in approximately 4% or more of the population. Examples of normal variants include webbing of the second and third toes and a single umbilical artery in an otherwise normal infant.

Terminology related to the formation of major anomalies

Malformation - A major anomaly that arises during the initial formation of a structure, i.e. during organogenesis. For most organs, this occurs during the first 8 weeks after fertilization. The resulting structure may be abnormally formed, incompletely formed, or may fail to form altogether. Examples of malformations include spina bifida and hypoplastic left heart. The term "congenital malformation" is also used more broadly to indicate any major anomaly.

Disruption - A major anomaly that results from alteration of a structure after its initial formation. The resulting structure may have an altered shape and configuration, abnormal division or fusion of its component parts, or loss of parts that were previously present. Examples of disruption defects include intestinal atresia and possibly gastroschisis.

Deformation - A major anomaly that results from molding of part of a structure, usually over a prolonged time, by mechanical forces after its initial formation. Examples of forces that may lead to a deformation include oligohydramnios (diminished amniotic fluid) and intrauterine crowding in twin, triplet, or higher order pregnancies. Examples of deformations include the compression (Potter's) facies seen with bilateral renal agenesis and some instances of clubfoot.

Terminology related to patterns of multiple anomalies occurring in a single child

Syndrome - A pattern of anomalies that form a specific diagnosis for which the natural history and recurrence risk are usually known. Use of the term "syndrome" implies that the anomalies have a common specific etiology. Examples include Beckwith-Weidemann syndrome and Rubinstein-Taybi syndrome.

Sequence - A pattern of anomalies that results from a single primary anomaly or mechanical factor. The presence of the initial anomaly or factor leads to one or more secondary anomalies, which may then lead to one or more tertiary anomalies, etc., in cascade fashion. Examples include Robin sequence (micrognathia; posterior displacement of the tongue; cleft soft palate) and oligohydramnios (Potter's) sequence (pulmonary hypoplasia; flattened facies; abnormal positioning of the limbs).

Association – A nonrandom pattern of anomalies that occur together more frequently than expected by chance alone, but for which no etiology has been demonstrated. Examples include VACTERL association (vertebral, anal, cardiac, tracheo-esophageal, renal, and limb anomalies) and CHARGE association (colobomas; heart defects; choanal atresia; retarded growth and development and/or central nervous system anomalies; genital anomalies and/or hypogonadism; ear anomalies and/or deafness). Use of the term “association” does not indicate that a specific diagnosis has been made.

Terminology related to tissue and organ formation

Agenesis - Failure of an organ to form.

Dysgenesis - Anomalous or disorganized formation of an organ.

Aplasia - Absence of a tissue or organ due to lack of cell proliferation.

Dysplasia – Disorganized cell structure or arrangement within a tissue or organ.

Hypoplasia - Undergrowth of a tissue or organ due to insufficient proliferation of otherwise normal cells.

Hyperplasia - Overgrowth of a tissue or organ due to excess proliferation of otherwise normal cells.

Terminology related to the timing of gestation and delivery

Embryonic period - The first eight weeks after fertilization during which most, but not all, organs are formed.

Fetal period - The period from the ninth week after fertilization through delivery.

Neonatal (Newborn) period - The first 28 days following delivery of a live born infant.

Prenatal - Before delivery.

Perinatal – Before, during, or after delivery. The exact time period may vary from 20 to 28 completed weeks of [gestation](#) through 7 to 28 days after delivery, depending on the context in which the term is used.

Postnatal - After delivery.

Terminology related to pregnancy outcome

Live birth – Spontaneous delivery of an infant that exhibits signs of life, including a heartbeat, spontaneous breathing, or movement of voluntary muscles. Transient cardiac contractions and fleeting respiratory efforts or gasps are not necessarily considered signs of life by all programs.

Fetal death (Stillbirth) – Spontaneous delivery of an infant or fetus at 20 weeks or greater gestation that does not exhibit signs of life. Transient cardiac contractions and fleeting respiratory efforts or gasps are not necessarily considered signs of life by all programs. A late fetal death is a fetal death that occurs at 28 weeks or greater gestation.

Spontaneous abortion (Miscarriage) - Spontaneous delivery of a fetus at less than 20 weeks gestation.

Induced abortion (Elective termination) - The purposeful interruption of pregnancy with the intention other than to produce a live birth and which does not result in a live birth.

Term infant - An infant born after 37 completed weeks and before 42 completed weeks of gestation.

Preterm infant - An infant born before 37 completed weeks of gestation.

Post term infant - An infant born after 42 completed weeks of gestation.

Low birth weight - Birth weight less than 2500 grams, regardless of gestational age.

Very low birth weight - Birth weight less than 1500 grams, regardless of gestational age.

Extremely low birth weight - Birth weight less than 1000 grams, regardless of gestational age.

Neonatal death - Death of a live-born infant within the first 28 days after birth. Early neonatal death refers to death during the first 7 days. Late neonatal death refers to death after 7 days but before 29 days.

Infant death - Death of a live-born infant before 12 months of age.

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