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What Birth Defects Are Common in Humans? How Are They Diagnosed at Birth?

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Congenital anomalies or birth defects are structural or functional abnormalities that occur during intrauterine life. Congenital anomalies can be diagnosed prenatally, at birth, or any time after birth. Structural birth defects are seen in about 1 of 33 infants within the first year of life and are the second most common cause of infant mortality, accounting for up to 25% of all perinatal deaths (prematurity is first). The frequency of structural birth defects is higher in spontaneous abortions than in live-born infants, reflecting that many of the most severe conditions are incompatible with survival. Functional congenital anomalies like intellectual disability or autism are infrequently recognized in infancy but are at least as common as malformations among older children and adults.

Genetic factors, including chromosomal abnormalities and single gene conditions, probably cause about half of all recognized congenital anomalies; environmental factors account for about 5%, while combinations of multiple genetic and environmental factors are thought to produce the rest. In this chapter we present a short discussion of some of the most commonly occurring major birth defects that are considered to be in this last category, i.e., of *multifactorial* origin. In general, multifactorial birth defects tend to be *isolated*, occurring as the only problem in an otherwise healthy child.

Congenital Heart Defects

Congenital heart defects (CHDs) are the most commonly recognized malformations, occurring in about 30% of infants with structural birth defects. These types of defects affect the heart chambers or walls, the heart valves and/or the blood vessels, causing the heart not to pump blood as efficiently as it should. Heart defects range in severity from mild conditions that may cause no symptoms and resolve with growth to severe, life-threatening malformations. In fact, CHDs are one of the most important causes of infant morbidity and mortality. Some common types of heart defects are ventricular septal defects, atrial septal defects, patent ductus arteriosus and Tetralogy of Fallot. Causes of CHDs include genetic factors (gene or chromosomal defects) and environmental factors including mother‘s exposure to certain medications, infections, or alcohol in pregnancy.

Diagnosis of CHDs can occur prenatally during a routine pregnancy ultrasound examination. When an abnormal heart is suspected, fetal echocardiography is usually performed to identify (or exclude) a specific heart abnormality. Sixty to eighty percent of severe heart defects are currently diagnosed prenatally. Some couples choose to terminate a pregnancy in which a serious CHD is diagnosed in the middle trimester, especially when the cardiac defect is associated with other birth defects or is recognized to be part of a chromosomal anomaly or other genetic syndrome. Recent improvements in the management of serious heart defects have led to many parents choosing post-natal surgical repair rather than pregnancy termination after prenatal diagnosis of CHD.

At birth, heart defects are suspected when a murmur is heard in the infant's heart or other abnormal signs, such as cyanosis, are found. Echocardiography is an important test for both diagnosing heart defects and following the problem over time.

Neural Tube Defects

Neural tube defects (NTDs) are a group of anomalies characterized by defective closure of the developing neural tube during the first month of embryonic life. A defect occurring in the upper end of the developing neural tube results in anencephaly (a lethal condition) or an encephalocele. However, a defect in the lower part of the developing neural tube, which produces spina bifida, an incompletely closed spinal cord and vertebral column, is more common. Patients with spina bifida may experience partial or complete paralysis of the lower limbs and impaired bladder and bowel continence. Upper limb involvement may also occur with lesions involving higher levels of the spinal cord.

Most NTDs are isolated defects due to multifactorial inheritance (interaction of genetic and environmental risk factors), with a recurrence risk of up to 4-5% in future siblings of an affected child in populations where NTDs are common, such as among Celtic, Hispanic, or South-Asian people. However, the risk of NTDs can be substantially reduced by maternal folic acid supplementation around and shortly after conception. In fact, the prevalence of NTDs fell sharply in North America following folic-acid fortification of flour. Other risk factors for NTDs include maternal obesity and pre-gestational diabetes mellitus.

NTDs, including all cases of anencephaly and most cases of spina bifida, can be detected prenatally through routine ultrasound examination. In addition, elevated levels of alpha-fetoprotein can usually be detected in the mother's blood by a screening test during the second trimester of pregnancy when the fetus has an NTD.

When an infant is born with spina bifida, the physician will assess the infant's motor and sensory functioning and perform imaging tests to assess the severity of spinal defect and the presence of associated problems elsewhere in the central nervous system. Corrective surgery is usually performed at birth for spina bifida and encephalocele, and additional rehabilitative, medical, or surgical treatments are typically required as the child grows older.

Orofacial Clefts

Cleft lip or palate occurs in about 1 in 700 births, with a higher frequency among Asian and Native American populations compared to African Americans. Cleft lip and palate are facial and oral malformations that usually arise between the fourth and seventh weeks of embryonic development, when the tissues do not join together properly, leaving a split in the lip (cleft lip) and/or an opening in the roof of the mouth (cleft palate).

Cleft lip is usually evident in a fetus on routine ultrasound examination during the second or third trimester of pregnancy. Cleft palate is often not identified until after the baby is born. Surgical repair of cleft lip can be performed in the third month after birth, while surgical correction of cleft palate is usually done at 6-12 months of age.

Genetic and environmental factors both play a role in causing these defects, and there is increasing evidence that maternal cigarette smoking and obesity during pregnancy may increase the risk for orofacial clefts in the baby, reinforcing the need for public health efforts to reduce these factors in women who are planning pregnancy.

Other Common Birth Defects

Other relatively common congenital abnormalities include limb deficiencies (missing or underdeveloped parts of limbs), extra fingers or toes (polydactyly), webbing between fingers and toes (syndactyly), club foot, incomplete closure of the urethra in males (hypospadias), and omphalocele or gastroschisis (defects in the abdominal wall). Most of these abnormalities are readily identifiable at birth, and some of them can be diagnosed prenatally by ultrasound examination.

Establishing the Diagnosis and Apparent Cause

Upon examination of a child with a malformation, the physician determines whether the abnormality is “isolated” or is one of multiple birth defects. Isolated defects are usually attributed to multifactorial inheritance, which may imply a higher recurrence risk for the same abnormality in future pregnancies. In contrast, when a common malformation occurs in association with other malformations, it is more likely to have a major genetic (chromosomal or single gene) or teratogenic cause. Chromosomal abnormalities are usually diagnosed with chromosomal microarray analysis. If a monogenic (mendelian) syndrome is suspected, exome sequencing or testing for one or more specific genes suspected of being involved may be performed. Teratogenic exposures of the mother during pregnancy produce characteristic patterns of abnormal growth and morphogenesis in the infant. In these cases, careful evaluation of exposure history and clinical evaluation by a specialist physician who is skilled in the assessment of birth defects is warranted.

Prevention

For both affected children and their parents, primary prevention of birth defects avoids tremendous suffering and costs. Primary prevention includes optimizing women’s health before conception by screening for and treating illnesses, eliminating cigarette smoking and abuse of alcohol or “recreational drugs” achieving a healthy body weight, and pursuing sufficient exercise and a healthy diet with folic acid and essential vitamin sufficiency.

If a child is born with congenital anomalies, understanding the potential causes can lead to more appropriate management and counselling, including the relief of anxiety or guilt, and provides families the opportunity to make future reproductive decisions that are better for them. The identification of a teratogenic cause informs the woman and her health care provider and offers the possibility of prevention of birth defects in future pregnancies.

Suggested Reading

Jones KL et al. Smith’s Recognizable Patterns of Human Malformation. Seventh Edition. Philadelphia: Elsevier Saunders, 2013

Stevenson RE et al. Human Malformations and Related Anomalies. Third Edition. Oxford University Press, 2015

Centers for Disease Control and Prevention (CDC). Birth Defects: https://www.cdc.gov/ncbddd/birthdefects/index.html

Centers for Disease Control and Prevention (CDC): Preconception care https://www.cdc.gov/preconception/index.html

Centers for Disease Control and Prevention (CDC): Developmental Disabilities https://www.cdc.gov/ncbddd/developmentaldisabilities/index.html

Pyeritz RE et al. Emery and Rimoin's Principles and Practice of Medical Genetics, Sixth Edition. Elsevier Science, 2013

On-line Mendelian Inheritance in Man: www.ncbi.nlm.nih.gov/omim