Fetal anomalies explained

Courtesy of Prof. Shane Higgins' website

Birth defects | Fetal anomalies explained

This feature lists and explains the most common birth defects. Below you can read some of the most frequently asked questions about birth defects, with links to the answers. Each common birth defect is listed and defined, helping you to understand about birth defects, also known as fetal abnormalities or fetal anomalies.

What are birth defects?

Also called fetal anomalies or congenital disorders, these pathologies are developmental disorders present at birth. These problems happen while the baby is developing inside the mother's uterus. **These anomalies may be structural, functional, metabolic, behavioural or hereditary.**

This is a global problem and is the leading cause of infant mortality. As teratologists explain, the first trimester of pregnancy is the most delicate one, because every single system of the fetus is beginning to form. For this reason, most birth defects happen during this trimester.

A common rule is that the earlier the developmental anomaly happens, the more major the birth defect is going to be. Most of the major defects lead to miscarriages/spontaneous abortions or neonatal deaths, and the rest lead to serious health issues. In counterpart, minor defects may not represent serious medical significance.

What is teratology?

Teratology is the branch of embryology and pathology that studies production, developmental anatomy and classification of malformed embryos and fetuses.

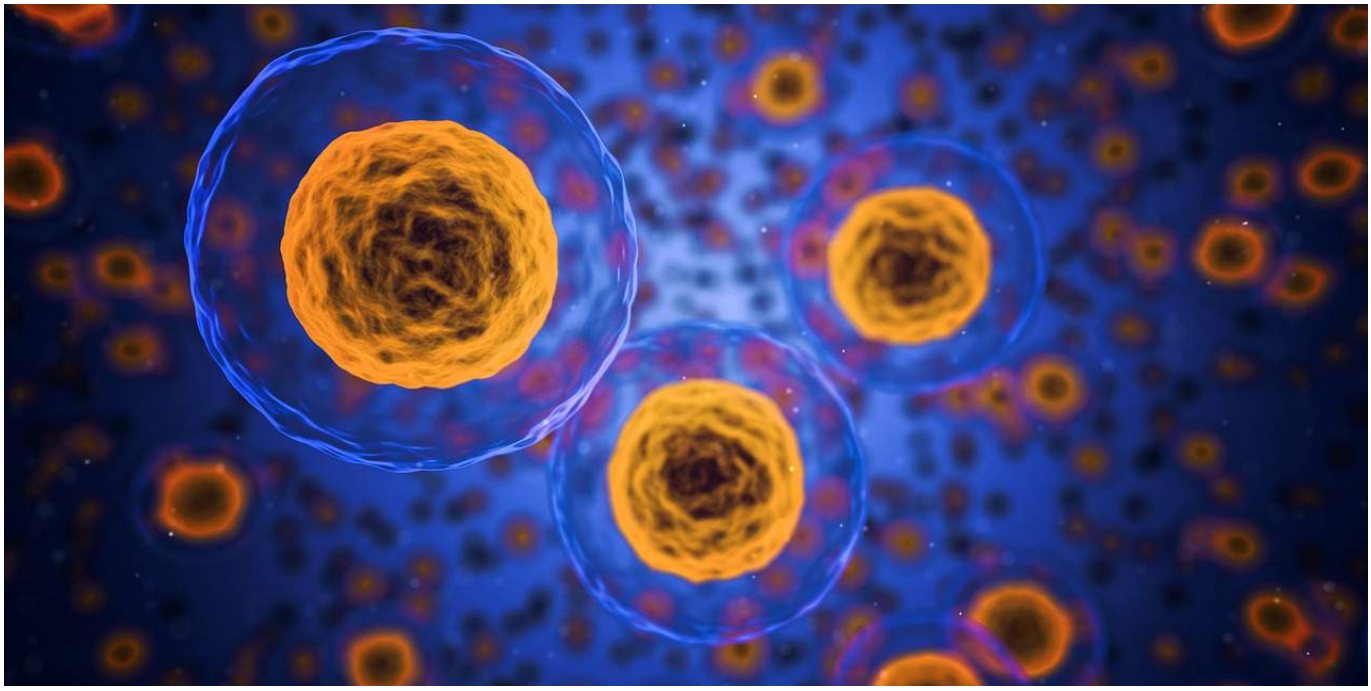
What are the main causes of birth defects?

Until the 1940s, people thought that embryos were protected from environmental agents such as drugs, viruses and chemicals by their extraembryonic or fetal membranes and their mother´s uterine and abdominal walls. In 1941, a reported case of the developmental malformations that an environmental agent (rubella virus) could produce to the unborn was documented.

In the 1950s, severe limb defects and other developmental disorders were found in infants of mothers, who had consumed a sedative (thalidomide) during early pregnancy. These discoveries focused worldwide attention on the role of drugs, viruses and environmental toxins as causes of human birth defects.

The causes of birth defects may be:

Genetics: during conception, the fecundated egg inherits one of each pair of chromosomes from each parent. If an error, either numeric or structural, happens during this process, it is going to lead to developmental anomalies from the beginning of formation.



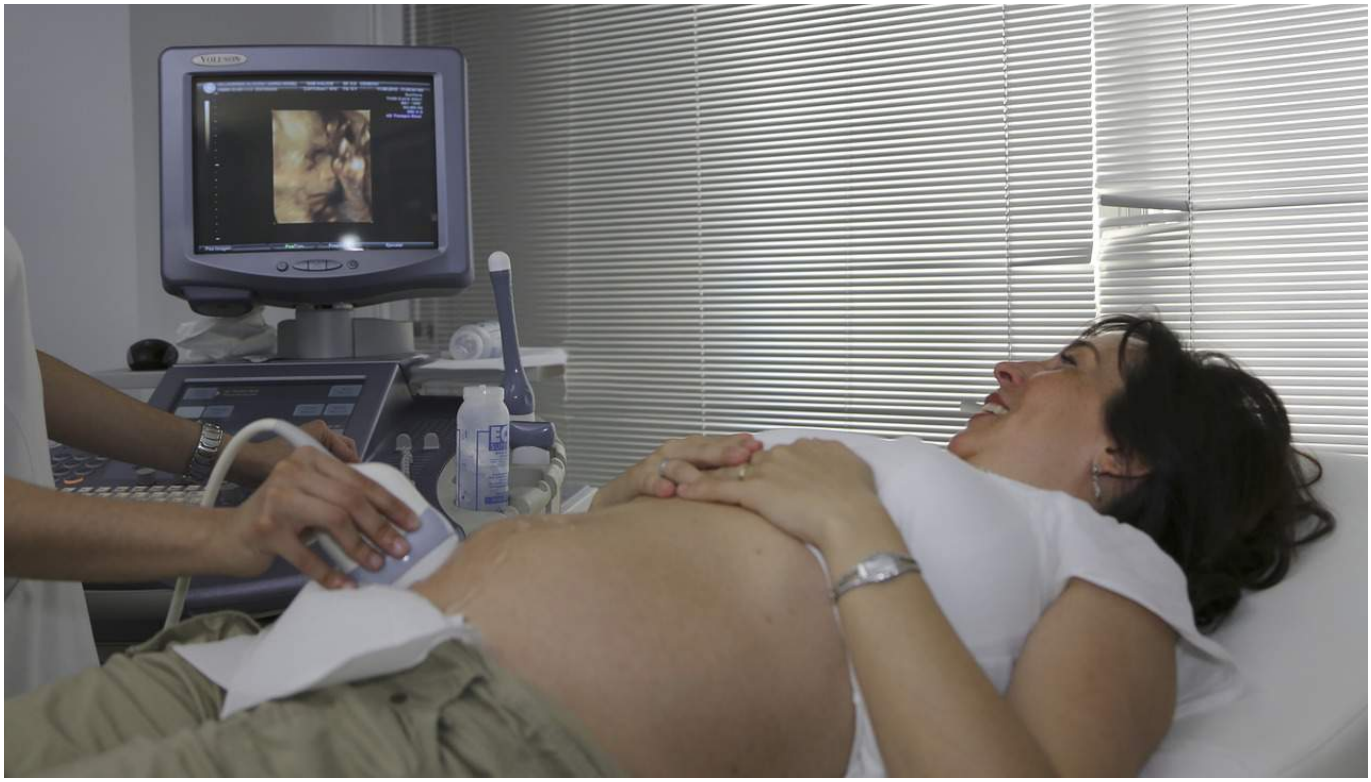
Environmental: certain infections such as toxoplasmosis, rubella and varicella during pregnancy can lead to these problems. Alcohol abuse and certain medicines that pass embryonic or fetal membranes can cause birth defects. The lack of consumption of certain vitamins, minerals and nutrients such as iron and folic acid, before and during pregnancy are also related to birth defects.

Multifactorial inheritance: genetic and environmental factors acting together.

Unknown: for 50% to 60% of birth defects, the cause is unknown.

How can birth defects be diagnosed?

Many birth defects are diagnosed during pregnancy through prenatal care with the help of an obstetrician-gynaecologist or a maternal-fetal medicine specialist. The prenatal care consists of providing regular consultations that allow the medical team to treat and prevent health issues of both mother and baby. In these consultations, the mother will receive medical information about pregnancy, from biological changes to prenatal nutritional guidance. Imaging diagnosis is a major tool used in this type of consultation.



What is a maternal-fetal medicine specialist?

Also known as a perinatologist, a maternal fetal specialist is a doctor who plays a major role in the life of complicated obstetric patients. This specialist performs imaging and prenatal tests with the purpose of discovering and, if possible, treating health issues that can compromise the life of the mother and/or the baby.

Birth defects-fetal anomalies caused by genetic factors

Genetic factors are the most important potential causes of birth defects. Mutant genes cause approximately one third of all birth defects. Two kinds of changes (errors) occur during chromosomic exchange: numeric and structural. These errors may affect the sex chromosomes (1 pair), the autosomes (22 pairs) or both. The abnormal mechanisms initiated by genetic factors may be identical or similiar to the causal mechanisms initiated by teratogens, such as drugs and infections.

Numeric chromosomal abnormalities

Normal human females have 44 autosomes (22 pairs) and two X chromosomes (a pair). Normal males have 44 autosomes (22 pairs) and, one X and one Y chromosome. Numeric aberrations usually result from non-disjunction during cell division (mitosis or meiosis), which results in an unequal distribution of one pair of homologous chromosomes to the daughter cells. One cell has two chromosomes and the other has neither chromosome of the pair.

Turner Syndrome

Also known as 45,X, Turner Syndrome is a pathology that affects only women and is based on the partial or complete absence of an X chromosome in some or all of the cells, leading to usually having 45 chromosomes. Almost 99% of fetuses with this syndrome spontaneously terminate during the first three months of pregnancy.

Patients may have a multiple list of signs and symptoms such as: broad chest, ears located lower than normal, short stature, swelling of the hands and feet, reproductive sterility, underdeveloped ovaries, amenorrhoea, absence of sexual maturation, obesity, webbed neck, cardiac malformations, horseshoe kidney, endocrine disorders, ophthalmic issues, attention deficit hyperactivity disorder, among other cognitive disorders. Diagnosis can be made by amniocentesis or chorionic villus sampling or abnormal imaging tests findings during pregnancy.

After birth, Turner Syndrome can be diagnosed based on symptomatology or karyotype. There is no cure for this pathology, but much can be done to minimise symptoms: growth hormone, oestrogen replacement therapy and reproductive technologies.

Klinefelter Syndrome

Also known as 47, XXY, this is a pathology that affects only males and is based in the existence of two or more X chromosomes besides to the Y chromosome, making the total chromosome number go to 47 or more.
Patients may present with reproductive issues such as sterility and small testicles. The symptoms may vary and be subtle or more prominent with low muscle strength, greater height, breast growth (gynecomastia), poor coordination, low libido and low testosterone levels. They also can present with cognitive and social disorders.

Diagnosis can be made by symptomatology (especially during adolescence) or karyotype. There is no cure for this syndrome, but the patients can receive hormone and behavioural therapy treatment.

Down Syndrome

Also known as trisomy 21, Down Syndrome is a chromosomic disorder produced by the existence of part or another third copy of chromosome 21. This syndrome is one of the most common genetic abnormalities. Important physical and intellectual disabilities represent the patients with this syndrome.

Patients may have a multiple list of signs and symptoms such as: slanted eyes, poor muscle tone, single crease of the palm, macroglossia, flat and wide face, short neck, toe malformations, short stature, low IQ levels (adult patients with the mentality of a child), delayed developmental milestones, risk of epilepsy, hearing and vision disorders, congenital cardiac, endocrine, gastrointestinal and reproductive issues.

Diagnosis can be made by ultrasound, amniocentesis, chorionic villus sampling and symptomatology. There is no cure for Down Syndrome, but the patients can receive education and proper care, to attain a good quality of life.

Edwards Syndrome

Also known as trisomy 18, is a chromosomic disorder produced by the existence of part or another third copy of chromosome 18. Many babies die before birth and survival beyond the first year of age goes from 5% to 25%.

Patients may have signs and symptoms such as kidney, cardiac, skeletal and gastrointestinal malformations, intellectual and developmental deficiency.

Diagnosis can be made by ultrasound with amniocentesis confirmation. Patients have to receive supportive treatment.

Patau Syndrome

Also known as trisomy 13, this is a chromosomic disorder produced by the existence of part or another third copy of chromosome 13.

Symptomatology can vary with intellectual disabilities, microcephaly, ophthalmic issues, central nervous system, musculoskeletal, cutaneous, kidney and cardiac malformations.

Diagnosis is based on clinical findings. Treatment focuses on the physical problems that these patients have.

Structural Chromosomal Abnormalities

Most of these abnormalities are the result of chromosome breakage, with the later reconstitution in a non-normal combination. The breakage may be induced by environmental factors such as ionising radiation, viral infections, drugs and chemicals.

The breakage can happen by translocation (transfer of a piece of one chromosome to a non-homologous chromosome), deletion (when a chromosome breaks, part of it may be lost), duplications (some abnormalities are represented as a duplicated part of a chromosome within a chromosome, attached to a chromosome or as a separate fragment), inversions (a segment of a chromosome is reversed) and isochromosomes (when the centromere divides transversely instead of longitudinally).

Cri Du Chat Syndrome

Also known as chromosome 5p deletion syndrome, this syndrome is caused by a partial terminal deletion from the short arm of chromosome 5 and affects infants producing a weak cat-like cry (produced by the existence of larynx and nervous system problems), feeding issues, microcephaly, abnormal facial features, low birth weight and poor growth, behavioural problems, severe mental deficiency, congenital heart disease, among other signs and symptoms.

Diagnosis is based on clinical findings. Treatment focuses on the physical and behavioural problems.

Birth Defects Caused by Mutant Genes

A mutation, usually involving a loss or change in the function of a gene, is any permanent, heritable change in the sequence of genomic DNA. The mutation rate can be increased by a number of environmental agents, such as large doses of ionising radiation.

Defects resulting from gene mutations are inherited according to Mendelian laws (laws of inheritance of single-gene traits that form the basis of the science of genetics).

Achondroplasia:

Produced by a mutation in the fibroblast growth factor receptor 3 gene, it may occur as a new mutation during the early stages of development or can be inherited from one parent. These patients may present with dwarfism, short proximal limbs, fingers and toes, normal size torso, large head with a prominent forehead, etc. Diagnosis is based on prenatal ultrasound, DNA tests and clinical findings. At the moment there is no known cure for the pathology.

Birth Defects Caused by Environmental Factors

The human embryo is well protected inside the uterus, but many environmental agents (teratogens) may cause developmental disruptions after maternal exposure to them. A teratogen is any agent that can disturb the development of an embryo or fetus. Environmental factors may simulate genetic conditions, for example, in cases when two or more children of normal parents are affected.

These factors cause between 7% and 10% of birth defects. Teratogens do not appear to cause defects until cellular differentiation has begun, however, their early actions may cause death of the embryo. The exact mechanisms by which these factors disrupt embryonic development and induce abnormalities remains obscure.

Many studies have shown that these factors affect embryonic development by altering fundamental processes such as the intracellular compartment, surface of the cell, extracellular matrix and fetal environment. It has been suggested that the initial cellular response may take place at a genetic, molecular, biochemical or biophysical level, resulting in different sequences of cellular changes leading to the final defect.

When considering the possible teratogenicity of a drug or chemical, three important principles must be considered:

1. Critical periods of development: the most critical period of development is when cell division, cell differentiation and morphogenesis are at their peak. Environmental disturbances during the first 2 weeks after fertilisation may interfere with cleavage of the zygote and implantation of the blastocyst and may cause early death/miscarriage of an embryo.

However, these are not known to cause birth defects. Development of the embryo is most easily disrupted when the tissues and organs are forming. The type of birth defect produced depends on which parts, tissues and organs are most susceptible at the time the teratogen is encountered.

2. Dose of the drug or chemical: for a drug to be considered a human teratogen, a dose-response relationship has to be observed and the greater the exposure during pregnancy, the more severe the phenotypic effect.

3. Genetic constitution of the embryo: studies show that embryos exposed to the same teratogen develop different defects or don't develop the effects at all. It appears that the genotype of the embryo determines whether a teratogenic agent will disrupt its development.

Body Walls Defects

Gastroschisis is:

A congenital fissure in the anterior abdominal wall that occurs in approximately 1 in 3000 live births and results from failure of the lateral body folds to fuse completely when the anterior abdominal wall forms during the fourth week of gestation. The site of the abdominal defects is to the right of the umbilical cord rather than truly in the midline. Part of the intestines come out through this defect and remains uncovered and floating in the amniotic fluid. An inflammatory peel may form secondary to this exposure. The liver and stomach may also come through.

Diagnosis is carried out by ultrasound scan.

Treatment/prognosis: Gastroschisis is usually managed surgically to return the exposed intestines to the abdominal cavity and close the hole in the abdomen. Untreated, this pathology is fatal.

Omphalocele is:

Herniation of abdominal contents into the proximal part of the umbilical cord persists. Omphalocele occurs in approximately 1 in 5000 births. Herniation of the liver and intestine may also occur. Herniated viscera are covered by a sac formed by peritoneum and amnion. The abdominal cavity of these patients is smaller because it does not have the pressure from viscera to grow. Omphalocele results from insufficient growth of muscle and skin components of the abdominal wall.

Diagnosis is by ultrasound

Treatment/prognosis: Omphalocele is usually managed surgically to return the exposed viscera into the abdominal cavity. It may be associated with other syndromes and birth defects of the cardiovascular and urogenital systems.

Facial Defects

Ocular Defects:

Many ocular defects involve the abnormal function of the retina (congenital detachment) or the non-development of the optic nerve, especially caused by infections by Toxoplasma gondii, rubella virus, herpes simplex virus, etc. in the first months of pregnancy or these defects may be linked to various syndromes.

Cyclopia:

Cyclopia is a rare defect which is the lack of existence of the two eyes and its partial or total combination forming a single middle eye in a single orbit. Usually it is associated with other craniocerebral defects which are incompatible with life.

Microphthalmia:

In microphthalmia the eyes are very small and are associated with other syndromes.

Treatment/prognosis: Depending on the severity of the case, surgery may be beneficial at a certain stage of life, in less severe cases. Prosthetics can be considered for more severe cases.

Anophthalmia:

Anophthalmia is the unilateral or bilateral absence of the eye with ipsilateral orbital defects.

Treatment/prognosis: Depending on the severity of the case, surgery may be beneficial at a certain stage of life, in less severe cases. Prosthetics can be considered for more severe cases.

Congenital Glaucoma:

Congenital glaucoma comes from the abnormal elevation of pressure inside the eye of neonates which usually results from a abnormal development of the aqueous humour's drainage mechanism during the fetal period.

Treatment/prognosis: Medical therapy and/or surgery.

Ear Defects:

Congenital deafness may come from the result of an abnormal development of the conducting conducts of the middle and external ears or an incomplete development of the structures of the inner ear. Many cases of congenital deafness happen because of genetic causes. It may be associated with other grave craniofacial defects. Minor external defects are common, especially in the auricle. Auricular appendages, anotia (absence of auricle), microtia (small auricle), atresia or absence of the external acoustic conduct are the most common.

Diagnosis: A special observation has to be carried out with patients who present with these kind of deformities to evaluate the condition, using ultrasound tests to examine the functionality and behaviour of internal organs, kidneys especially.

Treatment/prognosis: The majority of these external defects can be corrected with surgery.

Cleft Lip and Cleft Palate:

Clefts of the superior lip and palate are common facial birth defects. A 2015 report indicated that approximately 7000 neonates have orofacial clefts each year in the USA. These clefts are especially important because they result in an abnormal facial appearance and altered speech. Most clefts of the superior lip and palate result from a mixture of genetic and environmental factors, with each causing a minor developmental disturbance. These defects are the result of developmental failure of the union of frontonasal and maxillar protuberances. There are two main groups of this type of defect:

1. Anterior cleft defects, which include cleft lip and can include or not a cleft of the alveolar part of the maxillar bone. In a complete anterior cleft defect, this extends through the superior lip and alveolar part of the maxillar bone to the incisive foramen, separating the anterior and posterior parts of the palate.

2. Posterior cleft defects, which include clefts of the secondary palate that extend through both parts of the palate to the incisive foramen, separating the anterior and posterior regions of the palate.

The clefts vary from incomplete cleft lip to those that extend into the nose and through the alveolar part of the maxillar bone. Cleft lip may be unilateral or bilateral:

A unilateral cleft lip is the result of development failure of the maxillar bone protuberance on the affected side to unite with the fused medial nasal protuberances, resulting in a lip that is divided into medial and lateral parts.

A bilateral cleft lip is the result of development failure of the meeting between maxillar protuberances and fused medial nasal protuberances. There can be various degrees of defect on each side. This deformity is very important in terms of looks, because the orbicularis oris muscle loses its continuity (this muscle closes the mouth and purses the lips).

There is also a median cleft lip which is a rare case of this defect. Causes partial or complete failure of the medial nasal protuberances to merge and form the median palatal process. A median cleft of the inferior lip is also rare.

The cleft may involve only the end of the soft palate known as the uvula, or it may extend through both soft and hard parts of the palate. In grave cases in which is associated with cleft lip, this can extend through the palate to the alveolar part of the maxillar bone and both sides of lips. A complete cleft palate is the most severe degree of these cases. For example, a complete cleft of the posterior palate is a defect in which the cleft extends through the soft palate and anteriorly to the incisive foramen.

Clefts of the palate are classified depending on which side (anterior or posterior) of the incisive foramen is the defect:

- Clefts of the anterior palate.
- Clefts of the posterior palate.
- Clefts of the secondary parts of the palate.

Cleft lip and cleft palate may cause complications involving feeding, speech, ear disease (because of the abnormal position of the Eustachian tubes and external ear conducts) and social issues.

Diagnosis may be done with prenatal tests (ultrasound) by the obstetrician or perinatologist.

Treatment/prognosis: Surgery is the main treatment of these congenital malformation, depending on the grade of the pathology. Also, feeding techniques and speech therapy may be necessary posterior to the surgery.

Respiratory System Defects

Most common defects comes from the failure in the development of airways with abnormal recanalisation or abnormal communications between the conducts. Many of these congenital pathologies are not compatible with life without some kind of surgical intervention as soon as possible.

Laryngeal atresia is a rare defect which comes with the obstruction of the upper part of the fetal airway. Under this obstruction, lungs become enlarged and get filled with fluid due to ascites or hydrops. Also, diaphragm can present abnormal posture (flattened or inverted).

The tracheoesophageal fistula, the most common birth defect or the lower respiratory system, comes from the abnormal or incomplete division of the respiratory and esophageal parts during first weeks of development inside the uterus. This abnormality comes with serious gastrointestinal and respiratory complications due to the connection between these two systems. Gastric content may reflux and go directly to the lungs causing respiratory compromise. Tracheal stenosis and atresia are other abnormalities that are incompatible with life.

When it comes to lungs, agenesis is a very rare condition which comes from the total lack of development of one or both lungs. When the agenesis is unilateral, the condition usually is compatible with life, the mediastinal structures are moved to the side with no lung and the present lung is hyper-expanded. The bilateral agenesis is not compatible with life.

Lung hypoplasia refers to the low levels of development compared to normal ones. Lungs have a reduced volume and is associated with diaphragmatic abnormalities. Most cases are incompatible with life.

An accessory lung with no function may appear in some patients with these kind on pathologies.

Gastrointestinal System Defects

As a system made by conducts, many of the defects come from an obstruction or abnormal communication between them. From superior to inferior organs, esophageal atresia is the obstruction of the lumen, which is associated with tracheoesophageal fistula, which is the result of an incomplete separation of the oesophagus from the laryngotracheal conduct.

Isolated atresia comes from the non-recanalisation of the oesophagus during the second month of pregnancy.

Polyhydramnios (excessive amount of amniotic fluid) is a sign of esophageal atresia and it results as a complication due to the incapability of the fetus to swallow amniotic fluid. Neonates have excessive drooling and usually reject oral feeding with regurgitation and coughing.

The specialist can try to pass a catheter through the esophagus without having positive results. Diagnosis also can be done with imaging tests. With surgical intervention, the survival rate is very high. Esophageal stenosis can have similar and minor signs and symptoms.

Hypertrophic pyloric stenosis is a very common stomach defect in which there is an abnormal muscular thickening of the pylorus (distal sphincteric region of the stomach). This results in obstruction of the passage of food which produces the distention of the stomach leading to projectile vomiting from the baby. The treatment consists in the surgical relief of the pyloric obstruction.

Duodenal stenosis usually results from incomplete recanalisation of the duodenum. Because of this, the stomach contains bile and often produces vomiting. Duodenal atresia is the complete occlusion of the duodenal lumen due to the failure or complete recanalisation. Usually, the blockage occurs at the junction of the hepatopancreatic ampulla. Vomiting in neonates is not that premature as the esophageal atresia or hypertrophic pyloric stenosis are.

As in duodenal stenosis, the vomitus usually contains bile. The epigastrium looks distended. It is a pathology associated with other defects such as annular pancreas, cardiovascular and anorectal defects, and malrotation of the viscera. Diagnosis can be made based on the evidence of polyhydramnios and an ultrasound sign known as “double-bubble” which appears due to stomach and duodenum distention. Surgical intervention usually resolve the situation.

Birth defects of the intestine usually are very common. The majority of these defects present as malrotation of the gut, which results from incomplete rotation or fixation of the gut. Non-rotation of the mid-gut occurs when the intestine does not rotate as it re-enters the abdomen.

With this happening, the caudal part of the mid-gut loop re-enters to the abdomen first, putting the intestine on the abdomen in a transversal direction (small intestine on the right and the large intestine on the left side). The usual 270 degree counterclockwise rotation is not completed, and the cecum and appendix lie just inferior to the pylorus of the stomach, a condition known as sub-hepatic cecum and appendix.

The cecum is fixed to the posterolateral abdominal wall by peritoneal bands that pass over the duodenum. The peritoneal bands and the volvulus (twisting) of the intestine cause intestinal atresia. This malrotation happens due to failure of the mid-gut loop to do the final 90 degrees of the rotation.

When volvulus occurs, blood flow can be compromised, producing infarction and gangrene of the involved intestine region. Reversed rotation is the result of intestinal rotation in a clockwise direction rather than a counterclockwise one. Imaging studies can diagnose this malformation and surgical intervention is the right treatment.

Congenital megacolon, also known as Hirschsprung disease, is a very common pathology that results from aganglionosis in the distal bowel. These patients lack ganglion cells pertaining to the autonomic nervous system in the myenteric plexus after the dilated segment. The dilation comes due to incapability of relaxation of the abnormal segment, which prevents movement of the intestinal contents, resulting in dilation.

Diagnosis is based on imaging tests and pressure levels measure of affected intestine region. With surgical intervention, the patients may live a normal life. Most common anorectal anomalies involve imperforated anus, anal stenosis, membranous atresia, anorectal agenesis, anorectal fistulas and rectal atresia.

Urogenital System Defects

Congenital Anomalies of the Urinary System:

Defects in shape and position are the most common anomalies of this system.

Renal agenesis is the unilateral or bilateral absence of kidneys. Unilateral renal agenesis usually causes no symptomatology and is often not discovered until the earlier stages of life, due to the compensatory function provided by the present kidney. Unilateral renal agenesis should be suspected in infants with a single umbilical artery. Bilateral renal agenesis on the other hand, is associated with oligohydramnios (less than 400cc of amniotic liquid in the amniotic cavity as a result of little or no urine excretion). This condition appears once in 3000 births approximately and is incompatible with life.

Renal agenesis appears when the ureteric buds (the beginning of primitive ureters) do not develop or degenerate. Failure of these structures to penetrate the metanephrogenic blastemal resulting in a lack of kidney development because no nephrons (kidney's functional units) are induced by the collecting tubules for development.

Other abnormalities such as **malrotated kidneys** (abnormal rotation produced by an abnormal hilum, which as a result produces the abnormal situation of kidneys), **ectopic kidneys** (abnormal position produced by failure of the kidneys to ascend during development which results in pelvic, discoid, crossed or fused kidneys supplied by several vessels others than usual), **horseshoe kidneys** (kidneys´ poles are fused and its ascension during development is prevented by the root of the inferior mesenteric artery which holds them), duplications of urinary tract (produced by abnormal division of the ureteric bud) and ectopic ureter (a ureter that is not incorporated into the vesical trigone but into the urethra) does not produce much or severe symptomatology nor produces incompatibility with life. Minor signs and symptoms such as urinary incontinence may appear.

Diagnosis is mostly based on imaging tests and in some cases surgical intervention treatment may produce positive results.

Congenital Anomalies of the Genital System:

Hypospadias is the most common defect of the position of the external urethral orifice in the penis, which may come in four types: **glanular** (the most common type, the external urethral orifice is located on the ventral region of the penis´ glans), **penile** (the external urethral orifice is located on the ventral region of the penis´ body), **penoscrotal** (the external urethral orifice is located at the junction between the penis and scrotum) or **perineal** (the external urethral orifice is located between the unfused scrotum). This anomaly comes from the abnormal production of androgens by the fetal testicles or abnormal receptor sites for these hormones, resulting in failure of canalisation of fusion of urethral structures. In other cases, when the urethra opens on the dorsal region of the penis, the anomaly is called epispadias. Agenesis of external genitalia is extremely rare and in these cases, the urethra opens into the perineal region, near the anus.

Anomalies of the feminine genital apparatus are produced by the incomplete or abnormal development of paramesonephric ducts. Double, bicornuate or unicornuate uterus comes from the abnormal division of one or both paramesonephric ducts. Absence of vagina and uterus is rare (once in 5000 births approximately) and occurs from failure of sinovaginal bulbs to develop. Vaginal atresia or vaginal septum are anomalies that obstruct the vaginal canal. **Imperforated hymen** is the most common anomaly of the female reproductive tract system that results in obstruction.

Testicles may produce various anomalies, but the most important are: Cryptorchidism is the most common defect in neonates. By the end of the second trimester, the testicles should begin to descend into the scrotum using the inguinal canal. When this process does not happen, one or both testicles may remain within or just outside the abdominal cavity. In most cases, this pathology corrects by itself with the descent of the testicles by the end of the first year of life. If uncorrected, sterility and development of tumours may occur.

Ectopic testes appear because of the deviation of testes from their usual path of descent. These testes may arrive in other abnormal locations such as interstitial (most frequent), near the thigh or penis, or on the opposite side. Hydrocele is produced because of the passing of peritoneal fluid into the patent processus vaginalis which remains open during development.

Congenital Heart Defects:

Congenital heart defects are relatively common, with a frequency of six to eight cases every 1000 live births, and are a leading cause of neonatal morbidity. Some of these anomalies are caused by single-gene or chromosomal mechanisms. Others result from exposure to teratogens such as the rubella virus, however, in many cases the cause is unknown.

Imaging tests, such as real-time two-dimensional echocardiography, permit detection of fetal congenital heart defects as early as the 16th week. Most of these anomalies are well tolerated during fetal life, however, at birth, when the fetus loses contact with the maternal circulation, the impact becomes apparent. Some types cause very little disability, while others are incompatible with extra-uterine life. Because of recent advances in cardiovascular surgery, many types of congenital heart defects can be palliated or corrected surgically.

If the embryonic or primitive heart turns to the left instead of to the normal side (to the right), the heart and vessels are displaced in a reverse position. This is called **dextrocardia** and is one of the most common positional defects of the heart. In some cases, it is associated with situs inversus. Dextrocardia can usually be complicated with severe cardiac defects.

In **ectopia cordis** cases, the heart is located in a non-normal position. This may occur due to an incomplete fusion of the lateral regions in the thoracic wall formation during development (fourth week). The heart can be located in another position inside thorax or intra-abdomen. In most cases, death occurs very soon after birth. The clinical outcome for some of these patients has improved and many even arrive to adulthood.

In **atrial septal defects**, the most frequent type is patent foramen ovale, which has no clinical significance.

Other types of atrial septal defects with clinical significance include: **endocardial cushion defect** with **ostium primum defect, ostium secundum defect, common atrium** and **sinus venosus defect**. **Ventricular septal defects** are very common (25% of heart defects) and can occur in any region of the interventricular septum.

Among the types are: **membranous ventricular septal defects, incomplete closure of the interventricular foramen, muscular ventricular septal defects, absence of the interventricular septum. Persistent truncus arteriosus** comes from the failure of the aorticopulmonary septum and truncal ridges to develop normally and divide the truncus arteriosus into the pulmonary trunk and aorta. **Aorticopulmonary septal defect** is a very rare anomaly, where there is a connection between the aorta and pulmonary trunk close to the aortic valve.

Transposition of the great arteries is a frequent cause of **cyanotic heart disease** in newborns, usually associated with previous mentioned cardiovascular defects. This pathology involves the abnormal spatial arrangement of pulmonary artery and aorta. Transposition of the great vessels involves the abnormal spatial arrangement of venae cavae (superior or inferior), pulmonary artery and vein, and aorta. In these anomalies, deoxygenated blood keeps returning to the body because of the anatomic abnormalities. If uncorrected, patients with these anomalies usually die after months of age.

Tetralogy of Fallot includes four cardiac defects: **right ventricular hypertrophy, ventricular septal defect, pulmonary artery stenosis** and **dextroposition of the aorta**. Cyanosis is an obvious sign of the anomaly. Surgical repair is the treatment of choice in early years of life. The aortic valve or aorta itself may suffer of aortic stenosis (narrowing) or aortic atresia (complete obstruction). Coarctation of aorta is an aortic const
riction of various length in the region where the ductus arteriosus inserts, usually associated with Turner syndrome.

Professor Shane Higgins was part of a research team that studied, "Prenatal detection of structural cardiac defects and presence of associated anomalies: a retrospective observational study of 1262 fetal echocardiograms,2 in 2015. To learn more about this medical study, click on Professor Shane Higgins-Prenatal detection of structural cardiac defects and presence of associated anomalies..

Birth Defects Limbs:

Minor birth defects involving the limbs are relatively common and can usually be corrected surgically. Although these defects are often of no serious medical consequence, they may serve as indicators of more serious defects, which may be part of a recognisable pattern. The critical period of limb development is from 24 to 36 days after fertilisation. Major limb defects appear approximately 1 in 500 neonates. Most of these defects are caused by genetic factors.

There are two main types of limb anomalies or defects: amelia, which is the absence of a limb or limbs, and meromelia, which is the absence of part of a limb. In split-hand/foot malformations, a rare condition, there is absence of one or more central digits (fingers or toes) due to failure of development of one or more digital rays. The hand or foot is divided into two parts that oppose and curve inward. Brachydactyly is the shortness of digits (fingers or toes) and is caused by reduction in the length of the phalanges. Polydactyly is the presence of supernumerary digits (more than five digits on the hands or feet).

Syndactyly is a common birth defect of the hand or foot. Cutaneous syndactyly (simple webbing between digits) is more common in the foot than in the hand. It results from abnormal behavior of the webs to disappear between two or more digits. Osseous syndactyly (fusion of bones) occurs when the slots between the digital rays fails in development and as a result, separation of the digits does not occur.

Talipes equinovarus is a common birth defect (1 in 1000 births approximately) and it is the most frequent musculoskeletal deformation. It is characterised by an abnormal position of the foot which is inverted and its sole is turned medially. All anatomical structures are present, so the majority of cases can be treated with casting or taping. Developmental dysplasia of the hip occurs in approximately 1 in 1500 neonates and is a condition that appears because of the underdevelopment of the acetabulum of the hip bone and the head of the femur. Dislocation almost always occurs after birth.

Nervous System Birth Defects:

Spina bifida occulta comes from failure of fusion in the median plane of the halves of one or more neural arches (primitive nervous system). When present, it occurs in the vertebra L5 or S1. A small dimple with hair arising from it may be present in minor cases. Usually it does not produce symptoms, but some affected neonates may have neural symptomatology. The protrusion of the spinal cord or meninges, product of defects in the vertebral arches, is referred to as spina bifida cystica due to the meningeal cyst associated.

When the cyst contains portions of meninges, the defect is called **spinal bifida with meningocele**. If the cyst contains part of spinal cord or nerve roots the condition is called **spina bifida with meningomyelocele.** It has been associated with severe defects called **meroencephaly** which comes with inevitable death.

Depending on the extension and position of the defect, neurologic deficit may vary. High levels of alpha fetoprotein in the amniotic fluid strongly suggests the presence of meroencephaly. Ultrasound may also detect this defect.

Meningomyelocele is more frequent and more severe than spina bifida with meningocele. It may appear in any part of the vertebral column (most common in the lumbar and sacral portions). It is highly associated with hydrocephalus. **Myeloschisis**, the most severe type of spina bifida, occurs when the spinal cord is open because the neural folds failed to fuse. The affected spinal cord appears as a flattened mass of nervous tissue. Paralysis or paresis of lower limbs usually exists.

Abnormal development of the brain is common (3 cases every 1000 births). The factors causing these defects are genetic, nutritional and environmental. Abnormal histogenesis of the cerebral cortex can result in seizures and mental deficiency.

Encephalocele, a herniation of intracranial contents, results from a defect in the cranium., most common in the occipital portion of the skull. If it contains meninges, is called meningocele. If it contains meninges and portions of the brain, it is called meningoencephalocele. If it contains meninges, portions of the brain and part of the ventricular system, it is called meningohydroencephalocele.

Meroencephaly, a severe and common (statistics vary from 2 to 12 for every 10,000 live births) lethal anomaly of the calvaria and brain, comes from failure of the rostral neuropore to close during development. Forebrain, midbrain, portions of the hindbrain and calvaria are absent. **Exencephaly** (exposed brain) exists and the remaining portions of the brain are degenerated. **Acrania** (complete or partial absence of neurocranium) is always associated. Also, **rachischisis** (extensive failure of fusion of neural arches) may be associated.

Diagnosis is based on imaging tests.

Microcephaly, a neurodevelopmental disorder where the calvaria and brain are small, but a face appears with a normal size. Elevated mental deficiency is present. Exposure to large amounts of ionizing radiation, infectious agents (cytomegalovirus, rubella virus, Toxoplasma gondii, etc.) and certain drugs (maternal alcohol abuse) during fetal period are contributing factors in some cases.

Significant enlargement of the head is known as hydrocephalus, comes from an imbalance between the production and absorption of cerebrospinal fluid. Because of this, there is an excess of cerebrospinal fluid in the ventricular system of the brain. Most cases appear due to fetal viral infection or Toxoplasma gondii. Mental deficiency may result from various genetically determined conditions such as Down syndrome, action of a mutant gene or a chromosomal abnormality, maternal alcohol abuse, large doses of radiation, maternal and fetal infections such as syphilis, rubella virus, toxoplasmosis, cytomegalovirus, and congenital hypothyroidism.