

GENETICS



The term “genetics” describes the study of heredity. Hereditary characteristics are genetically passed from parents to children, as opposed to familial traits that may be passed through families, through rearing practices, or other factors in the environment. Thousands of characteristics, conditions, and diseases are known to be affected by genetics. Most recently, advances in biotechnology have provided the possibility of prenatal testing for the presence of these genetic disorders.



CATEGORIES OF GENETIC DEFECTS

There are three basic categories of genetic defects:

1. **Single Mutant Gene** This is one discrete unit of genetic material that is defective. Three patterns of inheritance are transmitted.
 - ◆ **Autosomal Dominant** The term “autosomal” applies to any gene present on a chromosome other than a sex chromosome (X, Y). The term dominant implies passage of a recognizable defect from a single parent to a child (risk rate 50%).
 - ◆ **Autosomal Recessive** The term recessive refers to a gene that does not produce a clinical effect unless an abnormal gene is received from both parents (risk rate 25 percent). Example of such diseases are cystic fibrosis, sickle cell anemia, phenylketonuria and color blindness.
 - ◆ **Sex-linked Genes** These are located on either the X (X-linked disorders) or the Y (Y-linked disorders) chromosomes. The female normally has two X chromosomes (XX configuration) and the male has one X chromosome (XY configuration). Y-linked disorders may be passed from father to son. X-linked disorders are passed from the father to a daughter.
2. **Chromosomal Abnormalities** These result from the lack of, excess of, or abnormal arrangement of one or more of the 23 pairs of chromosomes that produce either an excess or a deficiency in genetic material. Birth defects are an example of this relationship (risk is one in 250 newborns). Approximately 50 percent of miscarriages can be attributed to chromosome abnormalities.
3. **Multifactorial Inheritance** This is a process that occurs when an abnormal gene interacts with environmental factors to produce a congenital defect or disease. Examples are drugs and alcohol during pregnancy. Other conditions in this category are chronic diseases such as diabetes, coronary artery disease, schizophrenia, and some birth defects.



SEX DETERMINATION

Sex is determined by the matching of the 23 chromosomes from each parent. An embryo (conceptus) with two X chromosomes, one from each parent, develops as a female. An embryo with an XY (X from the mother, Y from the father) develops into a male.

GENETIC COUNSELING

Genetic counseling can be helpful before and during a pregnancy when there is a concern about a potential risk of an affected baby. Families with known genetic abnormalities can seek genetic counseling and testing for clarification of a disorder and also receive education about human inheritance. When confronted with a significant risk of a hereditary disorder, difficult decisions regarding management of a current pregnancy, and the prospects of planning a pregnancy, require a skillful expert who is thorough and sensitive to the person's culture. Tests that are commonly done in association with genetic counseling include:

- ◆ **Chromosome Analysis** Chromosomes can be cultured either from blood or body tissues, after which staining, banding, and counting the chromosomes are done to detect an abnormality. The chromosomes are photographed through a microscope, arranged in pairs, and then analyzed — a process called karyotyping.
- ◆ **DNA Testing** The ability to identify genes associated with diseases, as well as DNA markers, has made newer diagnostic tests available for a wide variety of disorders. An example of a condition detected with this technology is Huntington's chorea. These tests are kept confidential.
- ◆ **Newborn Screening** Newborns who are at risk for certain genetic disorders may be screened. This can be done for population-wide disorders or for individual concerns. An example of a population screening technique is PKU (phenylketonuria), which can identify infants who can be treated with diet to prevent mental retardation. There are now many screens available for consideration.



BIRTH DEFECTS

Birth defects may be inherited, developed during pregnancy, or caused during childbirth. The following are some of the more common birth defects:

BIRTH DEFECTS OF THE HANDS

■ POLYDACTYLY

This is the presence of an extra finger or fingers, most commonly a fifth finger or extra thumb. Surgery can remove the extra digit.

■ SYNDACTYLY

This is webbing of the fingers and can be corrected with surgery.

■ CAMPODACTYLY

This is the permanent bending of one or more fingers. It most often affects the little finger. Surgery can help correct this disorder.

■ CLUBHAND

This is a rare absence of the bone on the thumb side of the forearm or the larger bone on the opposite side of the forearm. The hand appears as a widened stump with stunted fingers. Treatment involves stretching the soft tissues of the arm during infancy. Several surgeries are often necessary.



BIRTH DEFECTS OF THE FEET

■ IN-TOEING AND OUT-TOEING

These are common problems in which the foot or leg turns inward or outward. This rarely requires treatment. The condition may be aggravated when the infant sleeps face down.

■ SYNDACTYLY

Webbing of the toes is rarely more than a cosmetic problem. The scars and contracture of the surgery may be more unsightly than the webbed toes. In contrast with webbed fingers, webbed toes will function normally.

■ CLUBFOOT

Clubfoot occurs in 1 out of 1000 births where the bones in the front of the foot are misaligned. In 95 percent of clubfoot deformities, the front half of the foot turns in and down. In the others, the foot turns out and up. Casts or splints in infancy may correct the disorder. In other cases, surgery is required.

BIRTH DEFECTS OF THE SKELETAL (BONES) SYSTEM

■ CONGENITAL DISLOCATION OF THE HIP

This is the abnormal development of one part or all parts of the hip joint in which the thigh bone does not fit into the hip socket. A brace or splint-like device to reposition the head of the thigh bone is used. This condition responds favorably to treatment.

■ DWARFISM (DYSPLASIA)

This is the abnormal underdevelopment of the body. Usually, the child's limbs are short and as the child grows, the trunk is also disproportionately short. There is no cure for this skeletal disorder, but there are orthopedic techniques to help the child function and to correct the deformities of the limbs and spine.

■ FUNNEL CHEST (PECTUS EXCAVATUM)

This is a deformity of the chest with the appearance of a sunken chest bone. It does not ordinarily affect breathing. Surgery is not recommended for children, but in adulthood it is often done for the sake of appearance. This is usually a congenital (existing at birth) defect, but also is caused by rickets.



BIRTH DEFECTS OF THE SEXUAL ORGANS

■ AMBIGUOUS GENITALIA

Ambiguous genitalia can manifest in several ways. Sometimes a female, who has been exposed to an excess of male hormones in the womb, is born with ovaries but male-like genitals. A male may be born with testes but with ambiguous or completely female genitals. The numerous cause may be chromosomal abnormality, or hormone excess or deficiency. Many times these disorders may be treated surgically after a correct diagnosis and the correct assignment of sex is established. Hormones may be used as well as reconstructive surgical procedures.

■ SUPERNUMERARY NIPPLES

Rarely, an infant is born with one or more extra nipples. The nipples may occur with or without breast tissue. They can be removed for cosmetic purposes.

BIRTH DEFECTS OF THE SEXUAL ORGANS IN BOYS

Abnormalities are not uncommon and some require treatment.

■ PHIMOSIS

A tightness of the foreskin that results in the inability to pull back the fold of skin that covers the uncircumcised penis. It can be congenital or the result of inflammation. Sometimes it requires minor surgical treatment or a circumcision.

■ PARAPHIMOSIS

This occurs when the foreskin of the penis is retracted too far and cannot be brought over the end. This can cause severe and painful swelling. When discovered early, the condition can be treated by gentle but firm pressure applied to the end of the penis to reduce the swelling and allow the foreskin to be brought to its normal place. Sometimes circumcision is required.

■ UNDESCENDED TESTES

This is the absence of one or both testes from the scrotum. The testis may be misplaced within the abdominal cavity or be absent altogether. This is rare. Occasionally, hormones are used to allow the testis to descend into the scrotum. Surgery is necessary if this is not successful.

■ HYPOSPADIAS

This occurs in approximately 1 in 500 newborns. The urethral opening is not in its normal position at the end of the penis. In its mildest form, the opening is just on the underside of the glans; in its most severe form, it may be as far away as the scrotum. The condition is treated surgically.



■ HYDROCELE

Hydrocele is the accumulation of fluid in an area of the testis called the tunica vaginalis. This is not uncommon in newborn boys. If the testes can be examined easily and the amount of fluid remains constant, treatment is unnecessary. Small hydroceles usually disappear during the first year. If the sac changes size during the day, it may mean there is a direct contact with the abdominal cavity. This indicates a hernia and does require surgery to repair the defect.

BIRTH DEFECTS OF THE SEXUAL ORGANS IN GIRLS

■ HORMONAL CHANGES

These changes occurring in the mother before birth often may cause changes in the breasts and genitals of the newborn daughter. This may be normal and temporary and require no treatment. Enlarged breasts sometimes occur in both girls and boys during the first two years of life due to the large amounts of circulating hormones that reach the baby through the umbilical cord. This is temporary and no cause for alarm.

The clitoris may also be temporarily enlarged due to hormone changes. The size decreases promptly following birth. Vaginal discharge sometimes occurs in the newborn. The discharge is the result of hormonal changes that took place in the mother. Treatment is unnecessary.

LIP AND PALATE DEFECTS

■ CLEFT LIP AND CLEFT PALATE

These defects may occur separately or together. Genetics seem to be more of a factor in cleft lip, with or without cleft palate, than cleft palate alone. An infant born with a cleft malformation, especially if it is a cleft palate alone, has a higher incidence of other defects, including hearing impairment. An infant born with a cleft lip has a fissure (slit) or elongated opening where the upper lip failed to fuse together. An infant born with either defect or both defects has an initial problem with feeding. A prosthesis can fit over the palate so the baby can be fed. Because of growth, this must be changed every few weeks. To close a cleft lip, surgery can be done at one to two months of age. If the opening extends to the nose, surgery is usually deferred until the child has reached adolescence. The cosmetic results depend on the severity of the deformity and the absence of infection.

The palate is closed within the first year of life to enhance normal speech development.



Complications of the defects include recurring ear infections, hearing loss, an excessive amount of dental cavities, and displacement of the teeth, which will require orthodontic correction. Speech therapy also may be helpful.

HEART DEFECTS

About 8 out of 1000 newborns have a congenital heart disorder. The precise cause of a congenital heart disorder is rarely found, although as a rule, multifactorial inheritance seems to be responsible. Recent advances in surgery provide the opportunity for many of the children to live normal lives.

■ VENTRICULAR SEPTAL DEFECT

This defect is the most common heart malformation (25 percent). There is an opening between the lower ventricles of the heart causing high blood pressure and an increased blood flow to the lungs. Small defects may close spontaneously. Many children manifest no symptoms or heart damage. Medical treatment is focused on controlling heart failure. Surgery, to close the defect, can be performed between one and two years of age, if necessary.

■ ATRIAL SEPTAL DEFECT

This is an opening high in the heart between the upper chambers (atria) that produces abnormal blood flow. The affected children often will have no symptoms. It occurs more often in children with Down syndrome. Surgical closure is usually done between three and six years of age.

■ PATENT DUCTUS ARTERIOSUS

This is the persistence of an opening in the vessel that leads from the pulmonary artery to the aorta (bypassing the lungs of the unborn fetus). Normally, this closes immediately after birth. When it does not, blood flows between the pulmonary artery and the aorta. It occurs often in premature babies, but in a full term infant, failure to close is a congenital malformation. A large ductus will produce a heart murmur, hypertension, and growth retardation. In the premature infant, the ductus often closes spontaneously. In a full term infant, whose ductus fails to close, surgery is usually necessary between the first and second year of life.



■ COARCTATION OF THE AORTA

This is a constriction of the aorta that results in increased blood pressure above the obstruction. There may be no symptoms. Heart failure may develop because of other associated heart abnormalities. The condition may be surgically corrected, usually between two and five years of age.

■ TETRALOGY OF FALLOT

This consists of a large ventricular septal defect, obstruction of blood flow from the heart's right ventricle to the lung (pulmonary) arteries, and a shift of the aorta to the right side of the heart. The physiological result is diminished blood flow to the lungs. The main symptom of this disorder is a bluish cast to the skin (cyanosis), although this may not always be present at birth. Treatment is focused on providing an immediate increase in pulmonary blood flow. Corrective open heart surgery is the usual treatment once the child is past infancy, or is occasionally necessary to improve the blood flow to the lungs and decrease cyanosis.

■ PULMONARY STENOSIS

This is an obstruction of blood flow from the heart to the pulmonary artery. Mild cases are without symptoms. Severely obstructed newborns have a bluish cast to the skin and show signs of heart failure. Mild obstruction can be carefully monitored and does not require treatment. More severe cases require surgery to correct the defect.

■ AORTIC STENOSIS

This type of stenosis is a narrowing of the valve through which blood leaves the heart to enter the aorta. Severe stenosis is usually detected in early infancy. Most children, however, have no symptoms. Surgery is needed for severe stenosis.

■ TRANSPOSITION OF THE GREAT VESSELS

This is a complex defect in which the two arteries arising from the heart are reversed. Blood returning to the heart from the body is pumped back to the body without passage through the lungs. Infants with transposition are blue (severely cyanotic) and must have immediate medical care. Surgical procedures are available for the condition.



DEFECTS OF THE CENTRAL NERVOUS SYSTEMS

These conditions occur in the brain and the spinal cord. A neurological problem in infancy is most likely due to a congenital malformation.

■ SPINA BIFIDA

Spina bifida is a defect in the failure of the vertebrae to close. This can occur with any vertebrae but most commonly occurs at the base of the back or lower spine. The defect can be surgically closed, but neurological deficits may not be correctable.

■ HYDROCEPHALUS

This is an imbalance between the brain's ability to produce spinal fluid and its ability to absorb it. An infant with hydrocephalus has an accumulation of fluid in the skull that produces an extremely large head. Sometimes medication is effective, but generally the best treatment is the surgical insertion of a shunt (tube) in the skull to drain the fluid. With treatment, the child may live beyond infancy, but many children have a deficit in motor and intellectual skills.

■ CEREBRAL PALSY

Cerebral palsy is the most common crippling disorder of childhood. (See Nervous Diseases chapter). It is caused by damage to the motor function areas of the central nervous system before, during, or after birth. There are many causes but the most common is the absence of adequate oxygen in the brain tissue (anoxia). There is no cure for cerebral palsy. The treatment involves early stretching exercises to help the muscles stay loose to improve mobility.

■ DOWN SYNDROME

This syndrome is a birth abnormality caused by the presence of an extra chromosome. An infant born with the disorder has a small, undersized, round head. The ears are set low and are oval. The eyes slant slightly upward. The mouth angles downward at the corners and tends to hang open. The tongue is usually enlarged and protruding. Most infants born with Down syndrome grow slowly and remain small. They have mental retardation that ranges from mild to severe. A woman's chance of giving birth to a child with Down syndrome increases with her age. Many children live with their family, go to school, and enter the work force in sheltered workshops or other low level jobs.



GASTROINTESTINAL DEFECTS

There are many congenital gastrointestinal abnormalities, the most serious of which obstructs the passage of food or fecal material. The most common defects affect the duodenum (first section of small bowel) or the rectum and anus.

■ PYLORIC STENOSIS

Pyloric stenosis is a narrowing of the pylorus, the part of the stomach through which food and other stomach contents pass to, or enter into the small intestine. The symptoms usually begin during the 2nd or 3rd week of life with possible mild vomiting. Usually the vomit contains no blood. The stools are small because little food reaches the intestines. Surgery should be performed as soon as possible and soon after, the child can begin normal feeding.

■ ESOPHAGEAL ATRESIA

This describes a condition where the esophagus (tube leading from the throat to the stomach) has not completely developed. The defect is not common. It is often accompanied by other abnormalities of the trachea or other life threatening problems of the heart, kidney, and central nervous system.

If the syndrome is found, immediate surgery is necessary. If the esophagus segment is underdeveloped and short, repair can be done immediately. If the segment is long, the surgeon may allow growth of the esophagus before attempting repair. In this event, a tube is placed through the abdominal wall into the stomach to permit feeding.

■ BILE DUCT ATRESIA

Bile duct atresia is an uncommon abnormality. It is difficult to differentiate between hepatitis and atresia. Other gastrointestinal abnormalities are often present. An exploratory operation may be necessary to determine the precise location of the obstruction. Rarely can it be corrected surgically, but drainage of bile can be achieved with a special connection to the intestine. Children usually have persistent inflammation of the liver and some require liver transplantation.

■ INTESTINAL ATRESIA

This causes an obstruction anywhere in the intestines. If the obstruction is high, vomiting is common. If the obstruction is lower, the abdomen becomes distended and tender. The treatment depends on the obstruction. A complete obstruction requires prompt surgery to prevent severe complications. Some minor obstructions require only medical management.



■ HIRSCHSPRUNG'S DISEASE (CONGENITAL MEGACOLON)

In an infant, this develops an abnormally enlarged or dilated colon. This condition is due to a failure of the lower rectum to propel the stool through the anus. The treatment is a procedure where an opening on the outside of the abdomen is created so that the stool can pass into a pouch placed on the outside (colostomy). This is temporary. A permanent surgical procedure to remove the pouch can be done between 12 and 18 months of age.

■ IMPERFORATED ANUS

This is seen when there is no opening into the rectum. Other defects often accompany this abnormality. Treatment depends on the location of the obstruction. If the opening is simply narrowed, it can be dilated. The degree of obstruction and a location higher in the rectum or colon requires a major surgical procedure with a temporary colostomy.

■ DIAPHRAGMATIC HERNIA

This type of hernia occurs when an abnormal opening in the diaphragm allows part of the abdominal contents to poke through into the chest cavity. In severe cases, the stomach and a large part of the intestines displace the heart and lungs. Surgery is necessary immediately.



ON THE HORIZON

Scientists continue mapping the genetic makeup of human beings, while individuals and organizations work to institute ethical guidelines. The Human Genome Project is a mission of the National Center for Human Genome Research at the National Institutes of Health (NIH). The goal is to map out the entire human Genome by the year 2005. The Genome is the sum of an individual's genetic material, which controls his or her heredity. The process has both positive and negative social implications. The ethical, legal, and social implications of the project have been accounted for through an organized program within the NIH and the Department of Energy called Ethical, Legal and Social Implications.