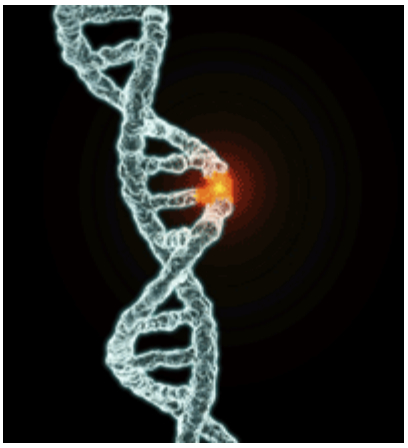
# Genetics in Special Education Series

## April 2011



## Genetic disorders presented in this issue:



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# Velocardiofacial Syndrome

### WHAT IS VELOCARDIOFACIAL SYNDROME?

Velocardiofacial syndrome (VCFS) is a genetic condition that is sometimes hereditary. VCFS is characterized by a combination of medical problems that vary from child to child. These medical problems include: cleft palate, or an opening in the roof of the mouth, and other differences in the palate; heart defects; problems fighting infection; low calcium levels; differences in the way the kidneys are formed or work; a characteristic facial appearance; learning problems; and speech and feeding problems.

The name velocardiofacial syndrome comes from the Latin words 'velum' meaning palate, 'cardia' meaning heart and 'facies' having to do with the face. Not all of these identifying features are found in each child who is born with VCFS. The most common features are palatal differences (~75 percent), heart defects (75 percent), problems fighting infection (77 percent), low calcium levels (50 percent), differences in the kidney (35 percent), characteristic facial appearance (numbers vary depending on the individual's ethnic and racial background), learning problems (~90 percent) and speech (~75 percent) and feeding problems (35 percent).

Two genes - COMT and TBX1 - are associated with VCFS. However, not all of the genes that cause VCFS have been identified. Most children who have been diagnosed with this syndrome are missing a small part of chromosome 22. Chromosomes are threadlike structures found in every cell of the body. Each chromosome contains hundreds of genes. A human cell normally contains 46 chromosomes (23 from each parent). The specific location or address of the missing segment in individuals with VCFS is 22q11.2.

VCFS is also called the 22q11.2 deletion syndrome. It also has other clinical names such as DiGeorge syndrome, Conotruncal Anomaly Face syndrome (CTAF), autosomal dominant Opitz G/BBB syndrome or Cayler Cardiofacial syndrome. As a result of this deletion, about 30 genes are generally absent from this chromosome.

VCFS affects about 1 in 4,000 newborns. VCFS may affect more individuals, however, because some people who have the 22q11.2 deletion may not be diagnosed as they have very few signs and symptoms.

## WHAT ARE THE SYMPTOMS OF VCFS?

Despite the involvement of a very specific portion of chromosome 22, there is great variation in the symptoms of this syndrome. At least 30 different symptoms have been associated with the 22q11 deletion. Most of these symptoms are not present in all individuals who have VCFS.

Symptoms include: cleft palate, usually of the soft palate (the roof of the mouth nearest the throat which is behind the bony palate); heart problems; similar faces (elongated face, almond-shaped eyes, wide nose, small ears); eye problems; feeding problems that include food coming through the nose (nasal regurgitation) because of the palatal differences; middle-ear infections (otitis media); low calcium due to hypoparathyroidism (low levels of the parathyroid hormone that can result in seizures); immune system problems which make it difficult for the body to fight infections; differences in the way the kidneys are formed or how they work; weak muscles; differences in the spine such as curvature of the spine (scoliosis) or bony abnormalities in the neck or upper back; and tapered fingers. Children are born with these features.

Children who have VCFS also often have learning difficulties and developmental delays. About 65 percent of individuals with the 22q11.2 deletion are found to have a non-verbal learning disability. When tested, their verbal IQ scores are greater than 10 points higher than their performance IQ scores. This combination of test scores brings down the full scale IQ scores but they won't represent the abilities of the individual accuarately. As a result of this type of learning disability, students will have relative strengths in reading and rote memorization but will struggle with math and abstract reasoning. These individuals may also have communication and social interaction problems such as autism. As adults, these individuals have an increased risk for developing mental illness such as depression, anxiety and schizophrenia.

## HOW IS VCFS DIAGNOSED?

VCFS is suspected as a diagnosis based on clinical examination and the presence of the signs and symptoms of the syndrome.

A special blood test called FISH (fluorescence in situ hybridization) is then done to look for the deletion in chromosome 22q11.2. More than 95 percent of individuals who have VCFS have a deletion in chromosome 22q11.2.

Those individuals who do not have the 22q11.2 deletion by standard FISH testing may have a smaller deletion that may only be found using more sophisticated lab studies such as comparative genomic hybridization, MLPA, additional FISH studies performed in a research laboratory or using specific gene studies to look for mutations in the genes known to be in this region. Again, these studies may only be available through a research lab.

## WHAT IS THE TREATMENT FOR VCFS?

Treatment is based on the type of symptoms that are present. For example, heart defects are treated as they would normally be via surgical interventions in the newborn period. Individuals who have low calcium levels are given calcium supplements and frequently vitamin D to help them absorb the calcium. Palate problems are treated by a team of specialists called a cleft palate or craniofacial team and again often require surgical interventions and intensive speech therapy. Infections are generally treated aggressively with antibiotics in infants and children with immune problems.

Early intervention and speech therapies are started when possible at one year of age to assess and treat developmental delays.

## IS VCFS INHERITED?

VCFS is due to a 22q11.2 deletion. Most often neither parent has the deletion and so it is new in the child (93 percent) and the chance for the couple to have another child with VCFS is quite low (close to zero). However, once the deletion is present in a person he or she has a 50 percent chance for having childen who also have the deletion. The 22q11 deletion happens as an accident when either the egg or sperm are being formed or early in fetal development.

In less than 10 percent of cases, a person with VCFS inherits the deletion in chromosome 22 from a parent. When VCFS is inherited in families, this means that other family members may be affected as well.

Since some people with the 22q11.2 deletion are very mildly affected, it is suggested that all parents of children with the deletion have testing. Furthermore, some people with the deletion have no symptoms but they have the deletion in some of their cells but not all. This is called mosaicism. Even other people have the deletion only in their egg cells or sperm cells but not in their blood cells. It is recommended that all parents of a child with a 22q11.2 deletion seek genetic counseling before or during a subsequent pregnancy to learn more about their chances of having another child with VCFS.

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# Turner Syndrome

## WHAT IS TURNER SYNDROME?

Turner syndrome is a chromosomal condition that alters development in females. Women with this condition tend to be shorter than average and are usually unable to conceive a child (infertile) because of an absence of ovarian function. Other features of this condition that can vary among women who have Turner syndrome include: extra skin on the neck (webbed neck), puffiness or swelling (lymphedema) of the hands and feet, skeletal abnormalities, heart defects and kidney problems.

This condition occurs in about 1 in 2,500 female births worldwide, but is much more common among pregnancies that do not survive to term (miscarriages and stillbirths).

Turner syndrome is a chromosomal condition related to the X chromosome. [ghr.nlm.nih.gov]
Researchers have not yet determined which genes on the X chromosome are responsible for most signs and symptoms of Turner syndrome. They have, however, identified one gene called SHOX that is important for bone development and growth. Missing one copy of this gene likely causes short stature and skeletal abnormalities in women with Turner syndrome.

## WHAT ARE THE SYMPTOMS OF TURNER SYNDROME?

Girls who have Turner syndrome are shorter than average. They often have normal height for the first three years of life, but then have a slow growth rate. At puberty they do not have the usual growth spurt.

Non-functioning ovaries are another symptom of Turner syndrome. Normally a girl's ovaries begin to produce sex hormones (estrogen and progesterone) at puberty. This does not happen in most girls who have Turner syndrome. They do not start their periods or develop breasts without hormone treatment at the age of puberty.

Even though many women who have Turner have non-functioning ovaries and are infertile, their vagina and womb are totally normal.

In early childhood, girls who have Turner syndrome may have frequent middle ear infections. Recurrent infections can lead to hearing loss in some cases.

Girls with Turner Syndrome are usually of normal intelligence with good verbal skills and reading skills. Some girls, however, have problems with math, memory skills and fine-finger movements.
Additional symptoms of Turner syndrome include the following:

- An especially wide neck (webbed neck) and a low or indistinct hairline.
- A broad chest and widely spaced nipples.
- Arms that turn out slightly at the elbow.
- A heart murmur, sometimes associated with narrowing of the aorta (blood vessel exiting the heart).
- A tendency to develop high blood pressure (so this should be checked regularly).
- Minor eye problems that are corrected by glasses.

- Scoliosis (deformity of the spine) occurs in 10 percent of adolescent girls who have Turner syndrome.
- The thyroid gland becomes under-active in about 10 percent of women who have Turner syndrome. Regular blood tests are necessary to detect it early and if necessary treat with thyroid replacement
- Older or over-weight women with Turner syndrome are slightly more at risk of developing diabetes.
- Osteoporosis can develop because of a lack of estrogen, but this can largely be prevented by taking hormone replacement therapy.

## HOW IS TURNER SYNDROME DIAGNOSED?

A diagnosis of Turner syndrome may be suspected when there are a number of typical physical features observed such as webbed neck, a broad chest and widely spaced nipples. Sometimes diagnosis is made at birth because of heart problems, an unusually wide neck or swelling of the hands and feet.

The two main clinical features of Turner syndrome are short stature and the lack of the development of the ovaries.

Many girls are diagnosed in early childhood when a slow growth rate and other features are identified. Diagnosis sometimes takes place later when puberty does not occur.

Turner syndrome may be suspected in pregnancy during an ultrasound test. This can be confirmed by prenatal testing - chorionic villous sampling or amniocentesis - to obtain cells from the unborn baby for chromosomal analysis. If a diagnosis is confirmed prenatally, the baby may be under the care of a specialist pediatrician immediately after birth.

Diagnosis is confirmed by a blood test, called a karyotype. This is used to analyze the chromosomal composition of the female. More information about this will be discussed in the section "Is Turner syndrome inherited?"

## WHAT IS THE TREATMENT FOR TURNER SYNDROME?

During childhood and adolescence, girls may be under the care of a pediatric endocrinologist, who is a specialist in childhood conditions of the hormones and metabolism.

Growth hormone injections are beneficial in some individuals with Turner syndrome. Injections often begin in early childhood and may increase final adult height by a few inches.

Estrogen replacement therapy is usually started at the time of normal puberty, around 12 years to start breast development. Estrogen and progesterone are given a little later to begin a monthly 'period,' which is necessary to keep the womb healthy. Estrogen is also given to prevent osteoporosis.

Babies born with a heart murmur or narrowing of the aorta may need surgery to correct the problem. A heart expert (cardiologist) will assess and follow up any treatment necessary.

Girls who have Turner syndrome are more likely to get middle ear infections. Repeated infections may lead to hearing loss and should be evaluated by the pediatrician. An ear, nose and throat specialist (ENT) may be involved in caring for this health issue.

High blood pressure is quite common in women who have Turner syndrome. In some cases, the elevated blood pressure is due to narrowing of the aorta or a kidney abnormality. However, most of the time, no specific cause for the elevation is identified. Blood pressure should be checked routinely and, if necessary, treated with medication. Women who have Turner syndrome have a slightly higher risk of having an under active thyroid or developing diabetes. This should also be monitored during routine health maintenance visits and treated if necessary.

Regular health checks are very important. Special clinics for the care of girls and women who have Turner syndrome are available in some areas, with access to a variety of specialists. Early preventive care and treatment is very important.

Almost all women are infertile, but pregnancy with donor embryos may be possible.
Having appropriate medical treatment and support allows a woman with Turner syndrome to lead a normal, healthy and happy life.

## IS TURNER SYNDROME INHERITED?

Turner syndrome is not usually inherited in families. Turner syndrome occurs when one of the two X chromosomes normally found in women is missing or incomplete. Although the exact cause of Turner syndrome is not known, it appears to occur as a result of a random error during the formation of either the eggs or sperm.

Humans have 46 chromosomes, which contain all of a person's genes and DNA. Two of these chromosomes, the sex chromosomes, determine a person's gender. Both of the sex chromosomes in females are called X chromosomes. (This is written as XX.) Males have an X and a Y chromosome (written as XY). The two sex chromosomes help a person develop fertility and the sexual characteristics of their gender.

In Turner syndrome, the girl does not have the usual pair of two complete X chromosomes. The most common scenario is that the girl has only one X chromosome in her cells. Some girls with Turner syndrome do have two X chromosomes, but one of the X chromosomes is incomplete. In another scenario, the girl has some cells in her body with two X chromosomes, but other cells have only one. This is called mosaicism.

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