22q11.2 Deletion Syndrome

Velo Cardio Facial Syndrome

DiGeorge

What is 22q11.2 Deletion Syndrome (Velo Cardio Facial Syndrome - VCFS)?

22q11.2 Deletion Syndrome (22q) or Velo Cardio Facial Syndrome (VCFS) is a genetic syndrome caused by a deletion of a small segment of the long arm of chromosome 22 (hence the name 22q11.2 Deletion Syndrome). It is suspected to be the second most common genetic disorder and occurs in approximately 1 in 2,000 births.

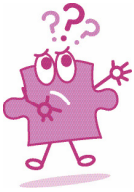
Getting a new diagnosis can be daunting, with a maze of information and medical professionals to navigate. We are here to offer information, education and awareness about 22q11.2 Deletion Syndrome.

22q has more than 180 physical and behavioural phenotypic features reported and can affect every body system.

22q is known by many different names, including Velo Cardio Facial Syndrome, Di George Syndrome or Sequence, 22q11 Deletion Syndrome, Shprintzen Syndrome, Conotruncal Anomalies Face Syndrome and Sedlackova Syndrome.

Most cases of 22q arise due to the deletion occurring for no apparent reason (de novo). This means no previous family member was affected. Other cases occur due to the deletion being passed on by a parent with the deletion; this is called autosomal dominant inheritance.

How is this 22q detected?



Genetic testing to confirm the 22q11.2 deletion is usually done from a simple blood sample sent to a clinical lab. The recommended test today involves methods that are more sophisticated than the previously used fluorescence in situ hybridization (FISH) as the new tests also can tell the size of the deletion or duplication. These include "genome-wide" method such as comparative genomic hybridization (CGH), a SNP microarray (e.g., CGA) or MLPA test. Again, targeted FISH studies can miss some smaller "nested" 22q11.2 deletions/duplications that the more sophisticated methods will detect. A standard cytogenetic test (karyotype) is only very rarely able to detect the 22q11.2 deletion in about 25% of cases and is therefore not a recommended method for detecting 22q11.2DS.

When should 22q11.2DS be suspected?

More than 180 anomalies have been reported in people with 22q11.2DS, but expression of the syndrome is highly variable from person to person and no individual has all of the anomalies. Also, some anomalies are readily apparent and may be recognized at birth while others are subtle and may go unnoticed until much later.

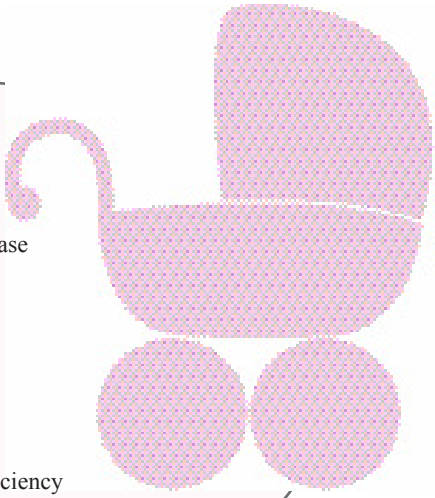
Still others are developmental and do not present until later on, such as learning disabilities. This explains why a diagnosis of 22q11.2 is sometimes made during the first few days of life, and other times, not until much later.

Also, there is great variability in the severity with which characteristics may appear and in the degree to which they cause difficulty. Each of these characteristics occur in isolation of each other and also can occur in other syndromes. It is when two or more of them occur together that a possible diagnosis of 22q11.2DS should be considered.

Facial Features

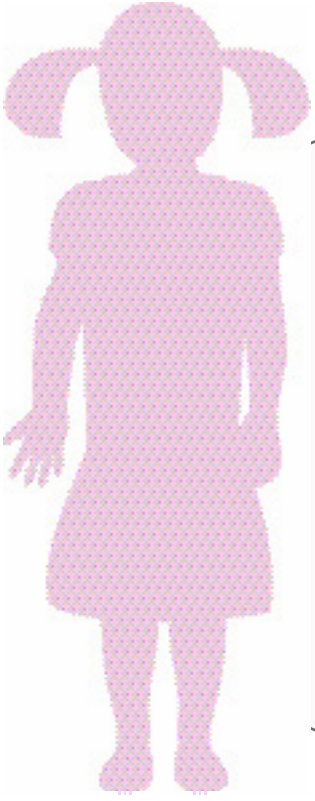
Although severe manifestations of the syndrome result in abnormal facial features, the large majority of individuals with 22q11.2DS are not at all unusual (dysmorphic) looking.

Individual facial features of 22q11.2DS represent minor anomalies or variants of normal that occur frequently in the general population so that they are not particularly distinctive.



Infancy

- Congenital heart disease
- Palatal abnormalities
- Feeding difficulties
- Immunodeficiency
- Hypoparathyroidism
- Renal anomalies
- Growth hormone deficiency
- Hernias
- Hypocalcaemia



Childhood

- Ear infections (otitis media)
- Developmental difficulties
- Speech & language difficulties
- Velo pharyngeal insufficiency
- Behavioural difficulties
- Leg pains
- Constipation
- Dental problems
- Vision problems
- Autoimmune disorders

Adolesence/ Adulthood

- Characteristic facial features
- Behavioural issues
- Ongoing medical issues
- Psychiatric issues

Who Should I contact if I suspect 22q

You can ask your General Practitioner (GP) or Paediatrician to refer you to a geneticist. They can perform a complete evaluation, discuss the testing and arrange for a genetic testing to be conducted.

CASE 1

MALE BORN 2000

INFANCY

Congenital heart disease

Soft palate cleft

Low set cupped ears

Overriding toes

Hernia

Weak cry

CHILDHOOD

Speech delay

Learning problems

Frequent ear infections

AGE OF DIAGNOSIS

2 weeks old

CASE 2

FEMALE BORN 1999

INFANCY

Poor feeder

Weak cry

Low birth weight

No facial expression

Rarely smiled

Lack of babbling

CHILDHOOD

Hearing impairment

Immune deficiency

Speech delay (grunting)

Velo pharyngeal insufficiency

Chronic ear infections

Hoarse voice

Visual impairment

Learning disability IQ <71

Constipation

AGE OF DIAGNOSIS

4 years old

CASE 3

MALE BORN 2004

INFANCY

Twin

Low birth weight

Poor feeder

Failure to thrive

Silent cry

Delayed milestones

Walked at 3

CHILDHOOD

Diagnosed with Autism

No speech until 4 years

Poor feeder and on oral supplements

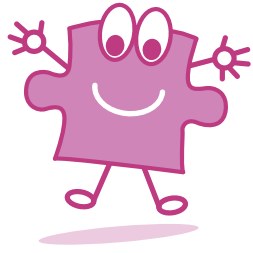
Chronic ear and chest infections

Reflux

Behavioural issues

AGE OF DIAGNOSIS

3 years old



Treating 22q11.2DS

There is no cure for 22q11.2, however, there are ways to treat many of the issues associated with the syndrome. It is very important to understand that each person's treatment should be done on a case by case basis as not all people respond to the same treatments or therapies. Some treatments are even syndrome specific. Palate, speech, immune system and attention issues are some areas in which treatment may differ.

A thorough evaluation of the individual with 22q11.2DS should be made to determine the best treatment. This includes evaluation by specialists relevant to the needs of the individual. Your Paediatrician or GP can co-ordinate your treatment and care plan.

LEARNING AND EDUCATION

Some form of developmental delay is present in over 95% of individuals with 22q11.2DS. Not all 22q individuals will be delayed to the same degree. Some fall into the borderline/mild category while others fall into the severe category. A developmental delay is present when your child has delayed achievement of one or more of their milestones. Milestones are a set of functional skills or age specific tasks that emerge over time, forming the building blocks for growth and continued learning. Your Paediatrician should screen for delays at your child's checkups.

Parents are usually the first ones to think that there is a problem with their child's motor, social, and/or speech and language development, and this parental concern should be enough to initiate further evaluation. However even if you do not think your child is developmentally delayed, regular assessment by a physiotherapist, occupational therapist and speech therapist are recommended for all children with 22q due to the high incidence of developmental delay associated with this syndrome. Inclusion in early intervention programs has shown to have large benefits for 22q children and reports from the above therapists will be necessary when applying for a position in such a program.

Many children with 22q have specific learning disabilities. Maths and abstract reasoning are typically most difficult. It may be helpful to place children in classes with fewer students within a program that can offer individualised instruction in areas of difficulty. Students' needs change over time as the curriculum becomes more complex and abstract. Parents should consult their local area health service or department of education to obtain a list of available services.

SPEECH AND LANGUAGE

Speech and language impairment is one of the most common clinical features in 22q11.2DS. The most common speech and language issues are: hypernasality, expressive language delays, articulation problems, auditory processing deficits, problem solving difficulties, reasoning difficulties, word finding problems, difficulty understanding idioms or words with multiple meanings and problems following multiple directions.

Hypernasality occurs when air escapes through the nose during the production of speech sounds resulting in reduced intelligibility. This is a common characteristic in the speech and language profile because 69% of children have palatal abnormalities. If the structure of the soft palate is such that it does not stop the flow of air from going up the nasal cavity, it will cause hypernasal speech. This phenomenon is referred to as velo pharyngeal insufficiency (VPI). Hearing loss can also contribute to increased hypernasality because children with hearing impairment can have difficulty self monitoring their speech.

Difficulties acquiring vocabulary and formulating spoken language (expressive language deficits) at the onset of language development are also common. Receptive language, which is the ability to comprehend, retain, or process spoken language, can also be impaired although not usually with the same severity as expressive language impairments. Articulation errors are commonly present in children with VCFS. These errors include a limited phonetic (speech sound) inventory and the use of compensatory articulation strategies resulting in reduced intelligibility.

EDUCATION AND SCHOOLING

Problems with education and schooling are one of the most common areas that parents worry about. It is essential that education be addressed from a very early stage, even before any problems are noted. Some children are able to go to mainstream schools with learning support while others may need a more nurturing environment. Making this decision can be difficult. Ask your child's therapists and preschool teachers their opinion on your child's development and coping skills. This may help you decide where your child would be best placed.

Telling the school about your child's diagnosis is recommended. This way the school can monitor your child's progress and apply for funding grants to get extra services to help in areas your child has difficulties with.

Monitoring your child's progress from an early age and giving them intervention as soon as a problem starts to surface has been shown to give a child the best start possible.

MENTAL HEALTH ISSUES

A number of young adults with 22q11.2DS have been found to suffer from mental health problems. Published psychiatric studies have presented some conflicting information, but it is safe to say that the majority of individuals with 22q11.2DS have some behavioural disorders which often begin after puberty when hormonal changes occur in the body. In most of these cases, the manifestations are not very severe and often do not require medical management. The frequency of severe psychiatric problems such as schizophrenia and bipolar disorder is fairly low, (reported under 20%), but the exact figure is not known. Part of the problem in psychiatric investigations is that the severity of psychiatric illness varies with age, typically becoming more apparent in adult life. However, not enough adults with 22q11.2DS have been studied to know the exact extent and severity of mental illness in this population, however this is changing.

SOCIAL IMPLICATIONS

22q affects the entire family and not just the affected individual. Mothers, fathers, siblings and extended family can all react differently to the diagnosis and it is important that all family members find the support they need. For some, reading about 22q and finding out as much information about the syndrome as possible can help, while others may want to know the bare minimum. Everyone copes differently and accepting this and giving each other time is important when a diagnosis is confirmed.

The 22q Foundation Australia & New Zealand has a wealth of information and we welcome you to contact us any time or visit the website www.22q.org.au.

Glossary

Autoimmune: An autoimmune disorder occurs when a person's immune system mistakenly attacks their own body tissues.

Congenital: Present from birth.

Echocardiogram: An ultrasound of the heart. It involves placing a small scanner on the chest wall, to take images of the heart. It is non-invasive and gives useful information not only about the structure of the heart but also the blood flow within it.

Electrocardiogram (ECG): Is a recording of the electrical activity of the heart. Numerous electrodes are attached to the chest wall to detect the hearts rate and rhythm.

Fluorescence In Situ Hybridisation (FISH): A test used to detect chromosomal abnormalities in cells.

Hereditary: A hereditary trait is that which can be transferred from parents to offspring. Therefore, a hereditary disease refers to a disease which can be passed on from one generation to another (i.e. it is inherited).

Hypocalcaemia: Abnormally low level of calcium in the blood; associated with hypoparathyroidism or kidney malfunction or vitamin D deficiency.

Hypoparathyroidism: Is a condition that develops when the parathyroid glands are unable to produce enough of a specific hormone that is needed to maintain the balance of calcium in the body.

Immune System: The immune system is responsible for the protection of the body against infection. It is divided into two parts: the innate immune system and the acquired immune system.

Immunodeficiency: A defect in the functioning of the immune system which renders the body more susceptible to illness.

Learning disability: A condition that either prevents or significantly hinders somebody from learning basic skills or information at the same rate as most people of the same age.

Murmur: Murmurs refer to abnormal heart sounds. Some murmurs are innocent while others may indicate a problem with the heart. An echocardiogram is performed to determine the type of murmur.

Paediatrics: Paediatrics is the branch of medicine that deals with diagnosis, treatment, and prevention of diseases in children.

Palate: The structure that forms the roof of the mouth. It consists of the anterior hard palate and the posterior soft palate.

Velo Pharyngeal Insufficiency: Is the improper closing of the Velopharyngeal sphincter (soft palate muscle) during speech characterised by an acute nasal quality of the voice.

22q Foundation Australia & New Zealand

www.22q.org.au

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The Foundation has an informative website with free downloadable information sheets and booklets as well as a coordination portal for families to use to coordinate their care.

22q

VCFS 22q11 Foundation

Australia and New Zealand