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KiDS-22q11 e.V.

Info

www.KiDS-22q11.de

22q11-Deletion

A Description of Syndrome 22q11

Kinder mit DeletionsSyndrom - 22q11 (KiDS-22q11) e.V., Blumenweg 2, 87448 Waltenhofen

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Kinder mit DeletionsSyndrom – 22q11 (KiDS-22q11) e.V., Blumenweg 2, 87448 Waltenhofen

is a self-help organization founded in 2001, which commits itself to children affected with the 22q11 (DS 22q11) deletion syndrome and their families. The 22q11 deletion syndrome is a genetic condition which in most cases occurs without an identifiable cause. It is characterized by a broad range of symptoms, of which only few apply to each individual affected.

The 22q11 deletion syndrome occurs in approximately every 4,000th case of childbirth, the condition is therefore often not discovered immediately. In the majority of cases the diagnosis is often made only after a heart abnormality is discovered, however, sometimes even later. The early discovery of the condition is very important to prevent or at least foresee possible complications which can then be treated accordingly.

The patients may only be guaranteed a high quality of life if holistic treatment can be provided on time. To achieve this end, patients, parents, and physicians should work hand in hand and dedicate themselves fully to the cause.

For these reasons the association provides the following:

- Regional contact partners and networking opportunity
- Youth group for children affected including their brothers and sisters
- Exchange of experience and information at regional and national meetings
- Semiannual information brochures / brochures on medical subjects
- Medical information from the scientific advisory council, meetings with experts
- Homepage: www.KiDS-22q11.com including various other services
- Internet forum with individual support in case of questions and problems
- Social law advocacy

ISSN: 1863-1576 V2 - 1. Edition. 2007 (1500 copies)
V2 - 2. Edition. 2008 (2500 copies)

22q11 (DS 22q11) Deletion Syndrome

- A Description of a Syndrome -

What is it?

The term “deletion” means that something is missing (derived from the Latin word *deletus* = deleted). In case of the 22q11 deletion syndrome, a piece of genetic material of one of the chromosomes 22 is absent at the location of q11.

Why do we need chromosomes?

Chromosomes are the packaging units of our genetic material. In each of them, several thousand genes are packed together. Our chromosomes help our cells to keep the genetic material in state of order, so to speak. According to most recent estimations our genetic material is composed of approx. 25,000 genetic dispositions, the so-called genes. In them, programs are encoded which make it possible for a human being to develop in all his diversity from a single fertilized egg cell. The subsequent function of our organs, our susceptibility to diseases, our behavior, and our intellectual abilities, i.e. our “dispositions and talents” are also co-determined by our genes. Genetic modifications are likely to produce deviations in the execution of the various development programs and functions. The consequence is mostly an organ development disorder which may already appear during pregnancy, however, physical functions that are of importance after the child is born may be affected as well.

Why do we need two copies of Chromosome 22?

We possess two copies of almost each of our genes and thus two copies of each chromosome we have, one from our mother and one from our father. For some genes it does not matter whether they occur once or twice. However, for a number of genes, particularly those which control embryonal development inside the womb, it appears to be very important that they occur in exactly the right dose, i.e. twice.

Which genes have been lost in the 22q11 (DS 22q11) deletion syndrome?

In most people with the 22q11 deletion syndrome approx. 3 million of approx. 3 billion existing building blocks carrying approx. 45 genetic dispositions are missing. This piece is only missing on one copy of chromosome 22, whereas the other is intact.
However, in some people smaller or other deletions exist which may be accompanied by a divergent set of problems. Some people occasionally display symptoms of the 22q11 deletion syndrome without having a deletion. Minute errors in a single gene, the TBX1 gene, were discovered in a group of them not identified in the course of regular "FISH analysis" screening (see next section).

How is the syndrome diagnosed?

The symptoms of the 22q11 deletion syndrome are diverse, but one by itself does not permit a diagnosis. The specialist will often be able to diagnose the syndrome tentatively, even in case of a slight manifestation, based on the minor peculiarities in the shape of the child's face (see below). However, the diagnosis will be corroborated only by proving the loss of genes on either one of the chromosomes 22. This is usually done in a blood sample, by means of a chromosome analysis and applying an additional fluorescence stain of the genetic material at the site of 22q11.2 (so-called "FISH analysis").

Specialist:
Human Geneticist

What effects does the 22q11 deletion syndrome have on a human being?

There are people who have an ascertained 22q11 deletion syndrome and are able to lead a completely normal life. These "carriers" of the genetic defect were often only identified once a 22q11 deletion syndrome had been found in an ill family member. Since healthy people are normally not examined, and since there have not been any systemic screening tests to date, it remains unknown how frequently the various problems associated with the 22q11 deletion syndrome actually occur.

In principle, the manifestation of the hitherto approx. 180 possible traits of the 22q11 deletion syndrome may strongly vary and they do not invariably possess significance in terms of an ill condition. The most frequently occurring problematic areas will therefore be represented in the following.

Heart /Blood Vessels

Malformations of the heart and the vessels close to the heart are a very typical manifestation of a 22q11 deletion. Owing to the modification in the genetic program, an erroneous process in cardiac development might already ensue at an early stage of pregnancy. One of the following conditions is then frequently observed. (The vessels conducting away from the heart are referred to as arteries, those conducting toward the heart are referred to as veins):

Interrupted aortic arch:
Type B: In this malformation of the major blood vessels, which is particularly characteristic of 22q11 deletion, there is no aortic connection between the descending left carotid and the left arm artery. If the vascular connection between the pulmonary artery and the aorta (ductus arteriosus), which still prevails before birth, closes as is usual in the first days of life, a life-threatening situation will arise, as vital organs will no longer be supplied with blood. This situation demands immediate intervention.

Ventricular septal defect (VSD): This defect in the ventricular septum generally represents one of the most common congenital heart malformations. If the defect occurs in a certain segment as is the case in Fallot's tetralogy it will be more often than not be found in cases of 22q11 deletion syndrome.

Pulmonary atresia including VSD: Here the connection between the right ventricle of the heart and the pulmonary artery is missing. Pulmonary blood circulation proceeds then through the ductus arteriosus or vessels which have been formed in compensation. In addi-

tion, there is a defect in the ventricular septum (VSD, see below) located at a typical site.

Fallot's tetralogy: This malformation includes an underdevelopment and constriction of the ejection tract belonging to the right ventricle, along with a constriction of the pulmonary artery (pulmonary stenosis). In addition, there is a typical ventricular septal defect (as in pulmonary atresia) which leads to a so-called “overriding” of aorta. Moreover, the wall of the right ventricle is thickened.

Truncus arteriosus communis: In this particular case, primarily the aorta and the lung artery have failed to separate from each other and consequently form one common blood vessel.

Course of the carotid artery: Sometimes the course of the cervical artery is seen to be altered. For this reason, retracing the course of the carotid artery is recommended prior to throat operations.

Specialists:
Pediatric Cardiologist, Heart Surgeon

Palatal Velum and Language

Alterations of the palate are very typical of people with the 22q11 deletion syndrome. Apart from the obvious malformations such as a cleft palate, there may also be concealed clefts lying underneath the mucous membranes. Even if none of these malformations exist, the velum often does not close properly and, for example, food might be discharged through the nose. This is referred to as "velopharyngeal insufficiency". If the palatal velum does not close properly when speaking, air escapes through the nose when sounds like “b” and “g” are formed making them sound nasal.

In general, a pronounced disturbance of speech and language development is frequently observed in infants with a 22q11 deletion syndrome. The problems are of extremely complex nature, since speech acquisition and production are affected at various levels. The children can often not be understood by third parties. The onset of speech development is strongly delayed and the vocabulary may then be extremely limited for many years.

Specialists:
Ears-Nose-Throat Physician, Oral and Maxillofacial Surgeon, Phoniatrician

Ears /Middle Ears

Patients with the 22q11 deletion syndrome often suffer from tympanic cavity effusions and recurrent middle-ear inflammations. The reason for this is an impairment of middle-ear ventilation through the Eustachian tubes (connection between middle ear and pharynx), for which various causes may exist. Firstly, malformations of the visceral cranium, secondly, alterations of the palate and palatal velum might permanently worsen the ventilation of the ear. The generalized susceptibility to infection, which often exists, also contributes to the contraction of middle-ear infections.

An above-average number of patients with the 2q11 deletion syndrome frequently suffer from an inner-ear hearing disability. Therefore an objective test for impairment of hearing should be performed, unconditionally and as early as possible (i.e. within the first months of life).

Specialists:
ENT Physicians, Pediatric Audiologists

Face/ Appearance

Many children typically have an oblong/narrow face, with a prominent nose and a broad root of the nose. The tip of the nose often appears to be relatively large due to the narrow nostrils. The attachment of the ears is rather low and the auricles are strongly folded inward. The mouth may be relatively small, the lips narrow, and the chin retracted. However, only seldom do the jaws display structural defects so severely that treatment will be necessary. 22q11 children often have an open mouth, for which the generally decreased muscle tonus and obstructed nasal breathing may be responsible.

Occasionally the mouth is slanted when the child screams, which is due to a unilateral underdevelopment of the muscles situated in the angle of the mouth. This may be mistaken for a paresis of the facial nerves, but mostly this has no great significance.

A delayed development of the dental buds and a late breakthrough of the permanent teeth has been noticed, however, this is without further consequences. A reduction of the dental enamel and its mineralization as well as individual missing dental buds have been observed, whereby the former lead to an increased occurrence of caries.

Specialists:
Orthodontist, Ear-Nose-Throat Physician, Oral and Maxillofacial Surgeon, Dentists

Immune System

Only few children with the 22q11 deletion syndrome have an impairment of the immune system which demands special measures to be taken against infections and/or a more complicated form of therapy. The 22q11 deletion syndrome may result in an underdevelopment and/or complete absence of the thymus gland The thymus gland is a small organ in front of the heart, which is responsible for the development of T /thymus) lymphocytes. T lymphocytes are important in the defense against fungi and viruses, but they also assist other immunocompetent cells in forming antibodies that ward off bacteria.

In addition, T lymphocytes have control functions that keep the immune system from directing itself against the own body (autoimmunity).

The underdevelopment of the thymus gland varies greatly in the 22q11 deletion syndrome. Even if thymus tissue is apparently missing (as can be seen during heart surgery, for example) a sufficient development of T lymphocytes is very often still possible, so that only a determination of the number and the function of T lymphocytes will really permit a conclusion as to whether and to which extent there might be a defect in the immune system.

This examination should proceed after diagnosis as soon as possible, since the outcome might necessitate protective actions to be taken (hygiene rules, antibiotic prophylaxis) and disclose whether the child may receive live vaccines (e.g. measles, mumps, German measles, or chickenpox) or if additional vaccinations are required.

If a blood transfusion should become necessary before the situation of the immune system is known (for example, in the scope of heart surgery), the donor blood must be subject to pretreatment.

Usually, there will be a gradual improvement of T cell development in the course of the first years of life. However, sometimes a disposition to autoimmune diseases (for example, juvenile rheumatism) will remain.

Specialist:
Immunologist

Urinary Tract

Children with 22q11 deletion syndrome sometimes display peculiarities affecting the urinary tract and the kidneys, which are mostly without consequences but may promote the development of urinary tract infections.

A urinary tract infection should therefore always be excluded in each case of unclear fever (in urine sample). In addition, an ultrasound scan of the kidneys is recommended in every child with the 22q11 deletion syndrome.

Bedwetting of the children affected is often complained of and is mostly the result of delayed maturation.

Specialist:
Nephrologist, Urologist

Diet

Even if structural alterations of the gastrointestinal tract are very seldom, disturbances affecting the uptake of food occur quite frequently. They may prevail individually or in combination and manifest themselves in the shape of low suckling strength, swallowing disorders, a reflux of food from the stomach into the esophagus. Most dietary problems result from delayed maturation and cease to exist later in life. Still, a failure to thrive at infant age, associated with a reduced weight and height increase, often exists.

In some cases transitory enteral nutrition might be necessary.

Specialists:
Specialist for swallowing disorders (dysphagia), Dietary Physician, Pediatrist with special training in dietary and digestive matters (Pediatric Gastroenterologist), Psychosomatic Physician

Hormones:

Growth: Delayed growth is frequently observed in 22q11 children, which is compensated before reaching adult age. Hormone-dependent growth disorders are of seldom occurrence. These children are typically of normal height at birth and then stay behind in their height development.

Calcium levels: An under-functioning of the parathyroid gland with subsequent strong depression of the calcium levels in blood occurs in some newborns with the 22q11 deletion syndrome. This may reveal itself, for example, in a tendency to convulsions or spasms.
As decreases of calcium values in the blood may also appear later, annual checkups with blood sampling are recommended. Since the magnesium levels might also be reduced concomitantly, this value should always be checked as well.

Specialist:
Endocrinologist

Skeleton

Some children with the 22q11 deletion syndrome display skeletal abnormalities. In particular, minor alterations of hands and feet occur. Due to the low muscle tonus (muscular hypotonia), an aberrant curvature of the spine (scoliosis) may occur at a later age, for which an early onset of therapy is important. It is recommended to check the functions of the cervical spine in children older than five years, in order to rule out the occurrence of instabilities in this part of the body.
The reason why leg pains occur in the 22q11 deletion syndrome (especially during the night) has not been ultimately explained. However, good experiences have been made with insoles adjusted to the feet and with physiotherapy.

Specialist:
Orthopedist

Mental Health

Mental diseases frequently occur in our society. People with the 22q11 deletion syndrome seem to be somewhat more affected than others.
Many who are affected by the 22q11 deletion syndrome have difficulties in the areas of communication which, apart from a purely lingual exchange of information, involve gesticulation and facial expression. They may lead to a reduced ability in the individual judgment of hazards, relationships, and social situations. In some cases a tendency towards anxiety, social withdrawal, and autistic behavior may follow.
The peculiarities typically appear up to the third year of life. An attention deficit / hyperactivity disorder is typically revealed at kindergarten age and presents a cause for difficulties particularly in school. ADHD seems to appear somewhat more often in children with the 22q11 deletion than in the normal population, which is particularly demonstrated in the easy distraction of the child.
Impulsive behavior is just as frequent. Disturbances of perception, mood, and motivation may appear especially after the onset of puberty. When mental diseases appear, it is important that the family becomes aware that they are not caused by mistakes made in parental child-rearing and that they can be treated with good results by support programs, behavioral therapy, and medication; the earlier they are identified, the better.

Specialist:
Pediatric Psychiatrist

Motoric Development

Most 22q11 children display a generalized weakness (hypotonia) of the muscles. This does not mean that there is a muscular disease, instead, the muscle tonus is decreased. Motoric development, i.e. the age at which the child is able to sit unassisted or walk, will therefore often be somewhat delayed.
An open mouth posture may also result from the reduced muscle tonus. However, this may also be the case if nasal breathing is obstructed.
A balance disorder is encountered in some children which will, for example, additionally make learning to ride a bicycle more difficult.

Learning Patterns

22q11 children often display a specific pattern of impaired partial performances, while other abilities may have developed normally. There may be spatial perception difficulties which lead to the learning disorder typical of the 22q11 deletion syndrome. In school, difficulties especially in mathematical subjects result therefrom.
As far as skills needed in everyday life are concerned, it may be that the execution of complex tasks will be more difficult.

Fitness for Life

Despite the fact that many 22q11 children display developmental retardation in many areas, they still continuously undergo further stages of development.

Some adults with the 22q11 deletion syndrome have already set the example, by leading a self-determined, regular life including gainful employment and starting a family. However, some children with pronounced learning disabilities will continue to require assisted care when they reach adult age.

Unless there is a serious heart malformation or an immunity defect as early as at birth, there has hitherto been no indication that the life expectancy of people with the 22q11 deletion will be reduced. Women with complex cardiac and vascular malformations, however, should seek competent medical counseling before pregnancy. For questions concerning hereditary issues there is the option of seeking genetic counseling.

Support and Sharing Life in a Community

Support and treatment should be adjusted to the needs of each person affected and his attachment figures. In this regard the general status of development and the specific problems must be considered, as well as his social environment (family, kindergarten, school, leisure time, occupation). An accurate assessment of findings (diagnostics) is recommended and can be particularly well conducted, coordinated and guided by the interdisciplinary team of a social-pediatric center (SPC), along with measures of support and treatment. An updated address list of SPCs can be found at www.dgspj.de.

Depending on the nature of the problem, physiotherapy, early intervention, occupational therapy, logopedics, speech therapy, or other pedagogic supportive measures are applicable.

The support of parents having to cope with burdens experienced or associated with 22q11 deletion is also of relevance.

Potentially necessary measures of family support, educational and social integration and contact persons in legal matters, and claiming disability compensation are also mediated by the relevant contact persons of the local SPCs.

The most important objective of all measures is to ensure the affected person's ability to share life in a community as good as possible and individually adjusted to his age and stage of development.

Specialist:
Social Pediatrist

How does a 22q11 deletion come about?

The loss of genetic material in the chromosomal region of 22q11.2 frequently occurs at random during the formation of egg or sperm cells, without either parent being personally affected. This is referred to as a "de novo" deletion. In this case, the likelihood is rather low that the same error should repeat itself. However, a 22q11 deletion may also have been genetically passed on to the child from one of its parents. Parents of a child with a 22q11 deletion can therefore undergo a test, consisting of a chromosome analysis of a blood sample, which will tell them if they had, or had not, a 22q11 deletion themselves. Further questions on genetic transmission and possibilities of prenatal examination can be answered in the scope of comprehensive interviews at a genetic counseling office. A list of advocacy centers in Germany is available at http://gfhev.de/de/beratungsstellen/beratungsstellen.php.

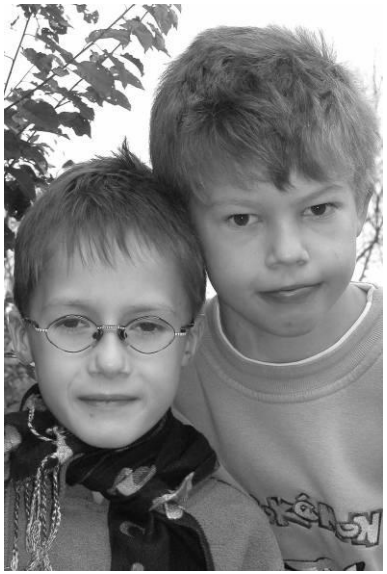
Why do other names for the 22q11 deletion syndrome still exist today?

The genetic defect responsible for the syndrome was first discovered in 1991 by Dr. Peter Scambler, a scientist in London, who had studied people suffering from the "DiGeorge Syndrome". The DiGeorge Syndrome comprises the collective appearance of severe heart malformations, a defective immunity due to underdevelopment of the thymus gland, and a calcium deficit due to a hypofunction of the parathyroids. However, in the course of time it was noticed that patients with similar conditions also had a 22q11 deletion syndrome. The other conditions are, for example, the conotruncal anomaly face syndrome, which describes the association between certain forms of heart malformations and characteristic facial features, the Shprintzen or velocardiofacial syndrome, emphasizing the difficulties associated between the velum and learning, or the Cayler-syndrome, in which an underdevelopment of the corner of the mouth is typical. As a consequence, the term CATCH 22 was suggested to encompass all diseases which were elicited by the 22q11 deletion syndrome. Each letter of the word stood for die one of the most frequently occurring symptoms, while 22 referred to chromosome 22. Since this designation was identical to a war satire and was felt to be discriminating, it is hardly used anymore.

How can we cope with it?

Presumably everyone will be initially shocked upon learning that his child or even he himself is “different”. However we must learn to accept that no human being is perfect and that disease may befall all of us at any given time. For most families a burden naturally arises due to concerns and the increased time effort to settle many things, but they do not have to affect one's life satisfaction. There are good treatment options for all the abovementioned problems, especially when these problems are identified at an early stage. Since multiple organ systems are often affected at the same time, the podiatrist, family doctor, or social podiatrist (SPC) will normally take over basic medical care and coordinate treatment. However, specialists in the respective fields will be necessary for certain issues.

Since the syndrome is very complex and each person affected may display various symptoms, it is sometimes difficult for many families, and for doctors and therapists as well, not to lose perspective. The registered association KiDS-22q11 e.V. and its medical advisory council hence commit themselves to provide information to experts, the persons affected and their families.



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Registered non-profit organization by the Tax and revenue Office in Kempten, Germany Tax ID No. 109/50677
Assoc. Reg. AG Kempten (Allgäu) VR 200148

Imprint: - “KiDS-22q11-Info Med Reports” issued by the Reg. Assoc.: Children with the 22q11 Deletion Syndrome. (KiDS-22q11) e.V. Blumenweg 2, 87448 Waltenhofen
- Reprint or reprint in part only with the express consent of the editor.
- Layout: Ulrich Geckeler

home: http://www.kids-22q11.com ISSN: 1863-1576 Printed in 01/2010

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Aufnahmeantrag in den Verein
Kinder mit DeletionsSyndrom 22q11 (KiDS-22q11) e.V.

V2.6 12/2007

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Vereinsregister AG Kempten (Allgäu) VR 200148

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Aufnahmeantrag

KiDS-22q11 e.V.

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