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The KDM5C syndrome

What is the KDM5C syndrome?
The KDM5C syndrome is a syndrome whereby children have a developmental delay in combination with a small height and some striking external characteristics.

What is the KDM5C syndrome also called?
The KDM5C syndrome is named after the place where a defect is present in the genetic material.

MRXSJ
Another word that is also used for KDM5C syndrome is MRXSJ. The letters MR stands for mental retardation, the medical word for developmental delay. The word X indicates that the error in the genetic material responsible for the development of this syndrome lies on the so-called X chromosome. There are now many different syndromes that cause a developmental delay due to an error on the X chromosome, the letters SJ of syndromic JARID1C are also added to this form. JARID1C is the parent name for KDM5C. That is why the combination of letters MRXSJ

Claes-Jensen syndrome
The Dutch name X-linked intellectual disability type Claes-Jensen is also used or simply the Claes-Jensen syndrome.

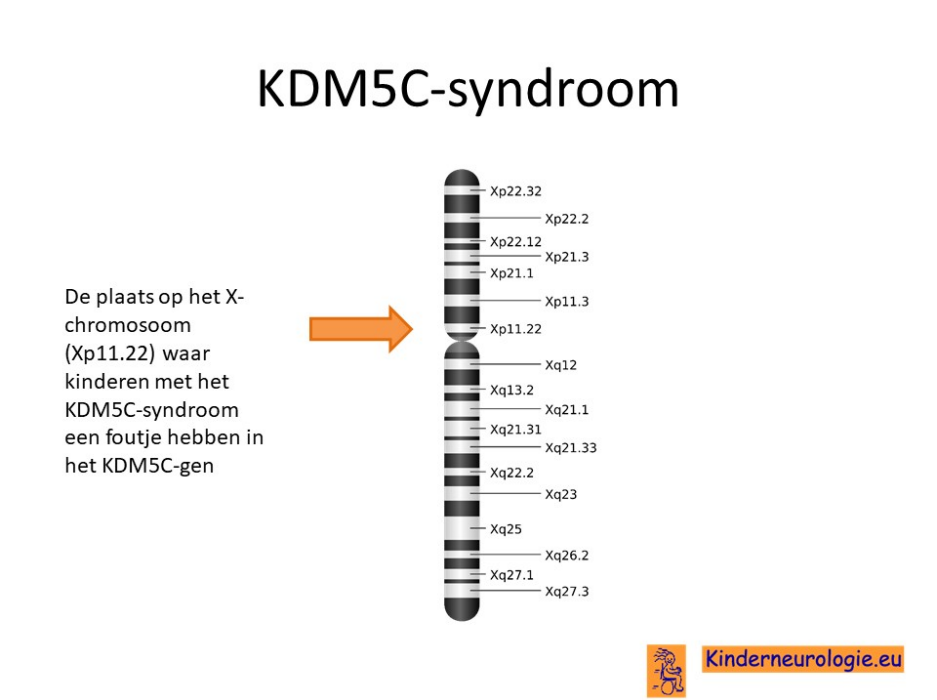
How often does KDM5C syndrome occur?
The KDM5C syndrome is a rare disease. It is not known exactly how often KDM5C syndrome occurs. The correct diagnosis has probably not been made for some of the children who have KDM5C syndrome either, because the syndrome has not been recognized.
New genetic techniques such as exome sequencing will probably make this diagnosis more often in children and adults with this syndrome.
It is estimated that KDM5C syndrome occurs in one in 35 to 140 people with intellectual disability due to an error on the X chromosome.

Here is room for your story

If your child has other symptoms, let us know.

In whom does the KDM5C syndrome occur?
The KDM5C syndrome has been present since birth. It may take some time before it is clear that there is KDM5C syndrome.
Both boys and girls can get the KDM5C syndrome. Boys usually have more symptoms than girls with this syndrome.

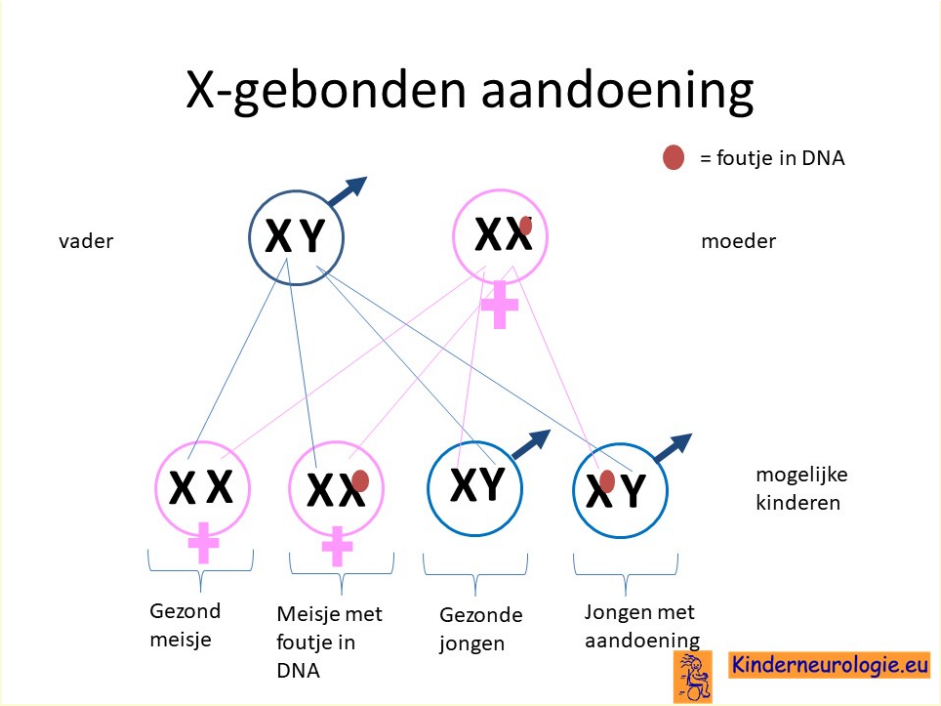
What causes the KDM5C syndrome?
Error in genetic material
The KDM5C syndrome is caused by an error on a piece of material on the X chromosome. The location of this error is called the KDM5C gene. In the past, the place in the genetic material was also called the JARID1C gene.



X-linked dominant
The KDM5C syndrome is caused by a so-called X-linked error. This means that boys, who only have one X chromosome, get more complaints when they have a defect in this KDM5C gene. Girls have two X chromosomes. If girls have an error in the X chromosome, then girls have another X chromosome without error. As a result, girls usually have problems to a much lesser extent than boys.

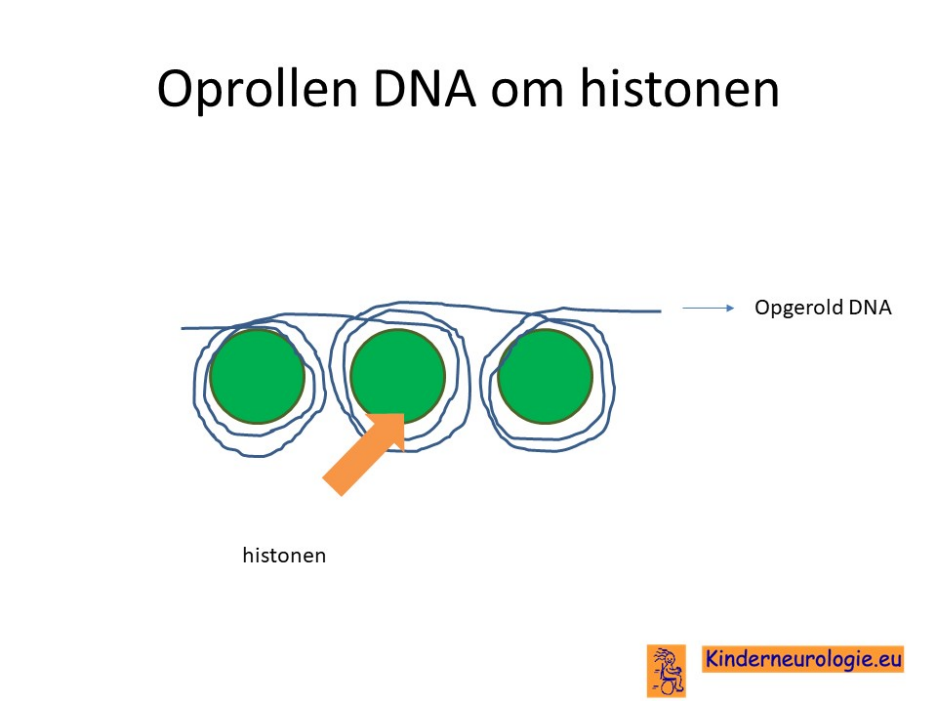
Originating in the child itself
In some of the children with KDM5C syndrome, the mistake occurred in the child itself after fertilization of the egg by the sperm and not inherited from one of the parents.

Inherited from a parent
Some of the children inherited the defect in the KDM5C gene from a parent, usually from the mother. This is because women often get fewer complaints as a result of having this mistake and therefore do not always know that they have a mistake in their genetic material.



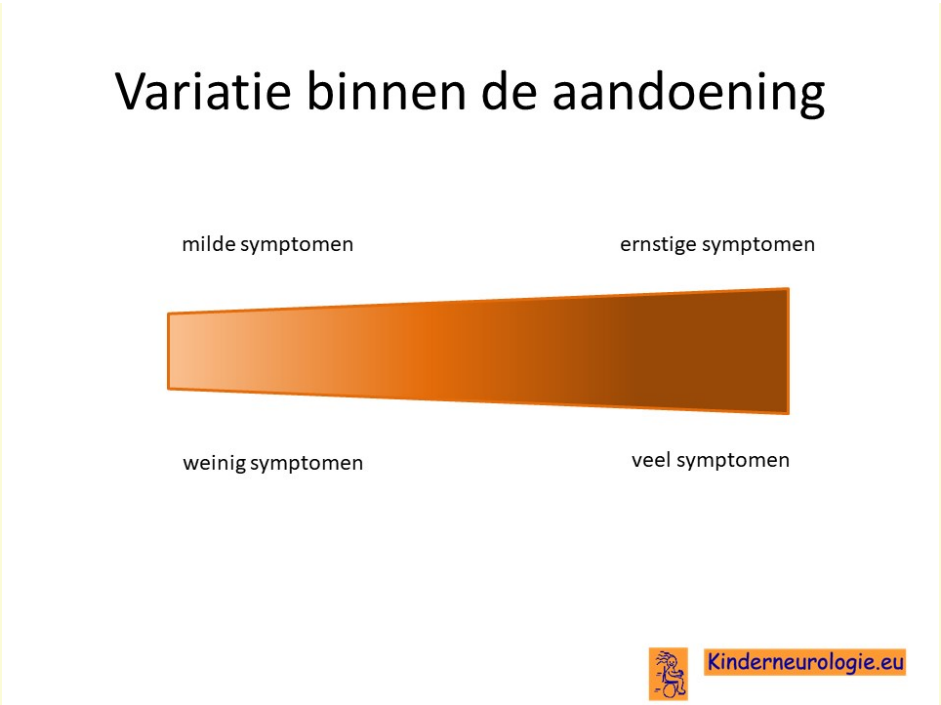
Aberrant protein

This piece of chromosome contains information for the production of a protein, called the Lysine (K) specific Demethylase C protein, abbreviated as KDMC protein. This protein plays an important role in folding and unfolding the DNA. Without this protein, the DNA is not properly folded and unfolded again, so that the information on the DNA cannot be read properly. The information on the DNA is important for the proper construction of the brain. As a result, the brains of children with this syndrome work less well than in children without this syndrome.



Construction of brain cells
Due to the inability to read the DNA properly, the brain cells are laid differently than usual. The brain cells take on a different shape, making the brain cells less able to transmit signals to other brain cells.

What are the symptoms of KDM5C syndrome?
Variation
There is a variation in the amount and severity of the symptoms that different children with KDM5C syndrome have. This is difficult to predict in advance which symptoms will bother a child. No child will have all of the symptoms below at the same time. Boys usually have more symptoms than girls.



Low muscle tension
Young children with KDM5C syndrome often have a low muscle tension, which makes them feel weaker. They must be well held and supported when they are lifted. Joints can easily be overstretched. Due to the lower muscle tension it is difficult for children to lift their heads. This is one of the reasons why children develop more slowly than other children.

Problems with drinking
Some of the babies with KDM5C syndrome have problems with drinking. They drink slowly and often release the breast or teat. It often takes a lot of time to breastfeed or bottle babies with this syndrome. With age, drinking is better for most children.

Developmental
delay Children with KDM5C syndrome develop more slowly than their peers. They later roll, sit and stand than their peers. Most children learn all this, but at a later age than their peers. Children with this syndrome fall easier than their peers. Children with this syndrome often have problems with fine motor skills, such as writing, drawing or cutting. This is much more difficult for them than for their peers.

Higher muscle tension
Gradually, children with this syndrome get a higher muscle tension in their body. This is mainly seen in the legs. In the beginning, this higher muscle tension helps children to stand on their legs and learn to walk. Later, the high muscle tension can make walking more difficult because of the stiffness in the legs. Children tend to cross their legs while walking, making it easier for children to fall. Children also often walk on their toes. Children have difficulty lifting their feet.

Problems with talking
For children with KDM5C syndrome it is difficult to learn to talk. The first words often come later than usual. For some of the children with this

syndrome it is not feasible to learn to talk. Most children have limited vocabulary in old age and find it difficult to make successful sentences. The sentences they make are often short and contain few words. Children with this syndrome often understand language better than speaking themselves.

Problems with learning
Children with KDM5C syndrome almost all have problems with learning. The degree of problems with learning differs, some children are difficult to learn or very difficult to learn. The IQs of the children who are familiar with this syndrome so far are between 40 and 70. This is called a slight to moderate mental disability.
Now that more and more children with this syndrome are becoming known with the help of new genetic techniques, it may well be that there are also children who have fewer problems with learning.

Autistiform characteristics
Children with KDM5C syndrome more often have autistiform characteristics. They are more introverted and do not have such a need for contact with other people. Children decide for themselves who they want to contact and who not.
Children with autistiform characteristics often like a fixed, predictable structure in the day. Children find it difficult when they deviate from this or when unexpected events take place. Children can become very angry or very sad because of unexpected events, because they do not know how to deal with this.
Children often prefer certain toys or a certain hobby that they can enjoy for a very long time, while they have little interest in other toys.

Friendly nature
Children with KDM5C syndrome often have a very friendly nature.

ADHD
AD (H) D is more common in children with this syndrome. Children have trouble keeping their attention for longer. They only play briefly with a certain toy and then with another toy. Children are easily distracted by a noise or movement in the room.
Children may have difficulty sitting still and prefer to move throughout the day. At school, children have trouble spending more time with school work.

Anxiety
Children with KDM5C syndrome suffer more easily from anxiety. For example fear of being alone without the parents, fear of the dark or fear of unknown and strange situations.

Aggression
Some of the children with this syndrome find it difficult to deal with anger. Children easily get angry when something goes different than expected or when something is not allowed. When children get angry, they also get very angry and they are very difficult to get out of it. In their anger, they can hurt other children or adults or themselves.

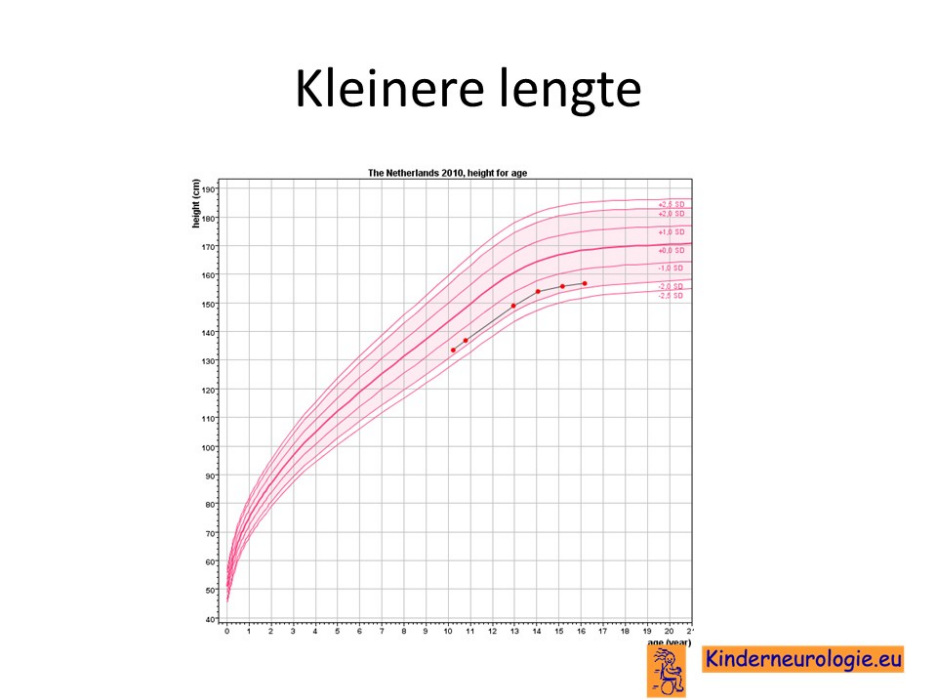
Epilepsy
Some of the children with KDM5C syndrome suffer from epilepsy attacks. Different types of seizures can occur.
This is strongly related to the age at which the child suffers from epilepsy.

Problems with sleeping Sleep
problems often occur in children with this syndrome. Some children have difficulty falling asleep. A large proportion of the children regularly wake up at night and then have difficulty getting back to sleep. Children are often awake early in the morning.
In some children, these sleeping problems are caused by epilepsy during the night.

External characteristics
With many syndromes, children often have some changed external characteristics. This does not bother children themselves, but it can help doctors to recognize that there is a syndrome and possibly also a syndrome. This also often means that children with the same syndrome often look more like each other than their own brothers and sisters, while the children are not related to each other.

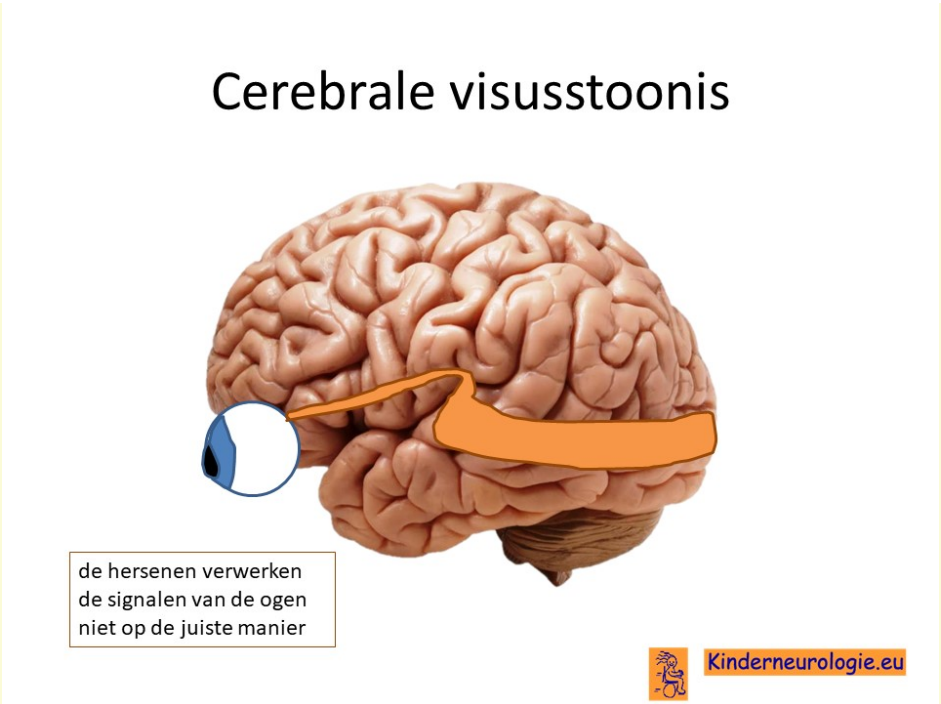
Children with KDM5C syndrome usually have no clear external characteristics. Some of the children have a smaller head than usual, while some of the children have a larger head. The forehead is often narrow. The eyebrows are short. The eyes are often deep and slightly lifted in the direction of the ears. The upper lip is thinner than the lower lip. The lower jaw and upper jaw are often small, many children have an overbite. The palate is often high. Deep grooves can be seen in the tongue. The teeth are often further apart in the mouth. The ears are often large, the earlobes slightly spiked. Children with this syndrome often have little facial expression. The fingers are often short and thick in relation to the rest of the hand. The feet are often small. A so-called funnel chest,

Growth
Children with KDM5C syndrome are usually a lot smaller than their peers. They belong to the category of the 3% smallest children in their age category. As a result, children with this syndrome are often estimated to be younger than they actually are.



Hair
A part of the children has more body hair than usual. The main hair can show bald spots.

Problems with seeing
Some of the children with KDM5C syndrome have low vision, they see blurred.
Sometimes this is due to a problem with the eyes, some of the children are short-sighted or presbyopic and need glasses. Strabismus often occurs in children with this syndrome.
Part of the problems with seeing is not due to a problem of the eyes themselves, but due to the brain malfunctioning. The brain does not or not properly process the stimulus that the eyes transmit, which means that children can see poorly. This is therefore called a cerebral vision disorder , the problem is in the brain (cerebrum), it is also abbreviated as CVI (in the English terms cerebral visual impairment, impairment is limitation).



Club feet
Part of the children with this syndrome are born with club feet.

Plasser
Boys with this syndrome often have a small pee and small testicles. For some of the boys, the balls did not descend properly into the ball bag.

Cleanliness
Most children with KDM5C syndrome become toilet-trained at a later age than usual.

Constipation
Constipation of the intestines is common in children with this syndrome. The stool does not come every day and is often hard, so children have trouble defecating. This can cause stomach pains.

More prone to infections
Children with KDM5C syndrome are more prone to getting infections at a young age. Airway infections or ear infections occur regularly.

Girls
Girls who have an error on the X chromosome in the KDM5C gene have another X chromosome without error. This allows girls to have complaints to a lesser extent than boys, but sometimes they have as many complaints as boys.

How is KDM5C syndrome diagnosed?
Story and research
Based on the story of a child with a developmental delay and some striking external characteristics, it can be suspected that there is a syndrome. However, there are many different syndromes that can all cause these symptoms. Additional research will often be needed to diagnose KDM5C syndrome.

Blood tests
Routine blood tests show no details for children with KDM5C syndrome.

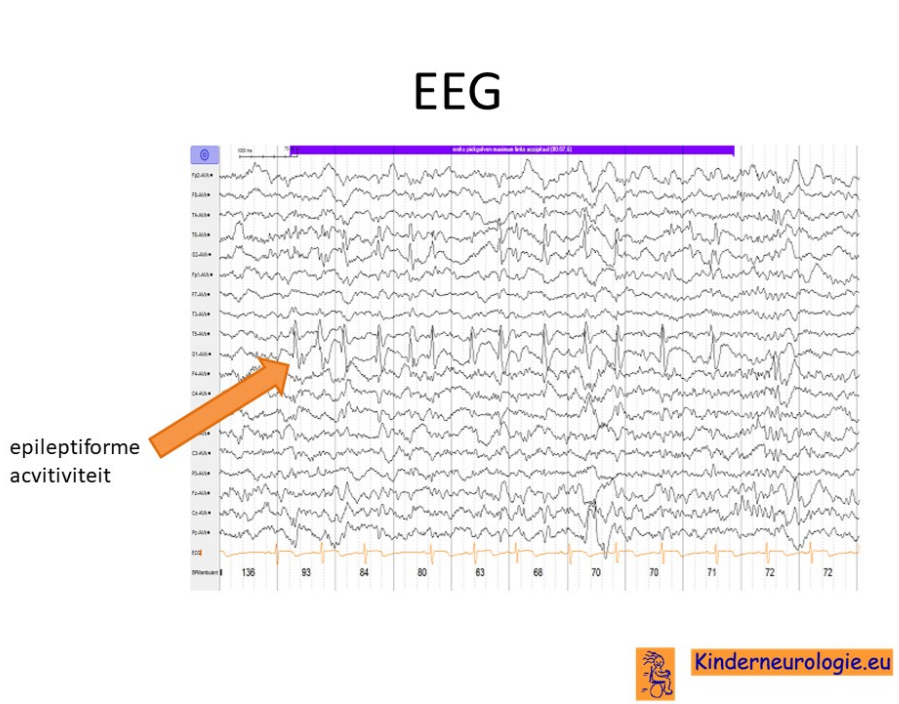
Genetic testing
When the diagnosis is considered because this disorder occurs in the family, targeted genetic testing on blood can help to prevent an error on the X chromosome in the KDM5C gene.
Often all chromosomes are examined at the same time (so-called Array examination), sometimes KDM5C syndrome can be diagnosed this way because it

is discovered that a part of the X chromosome on which the KDM5C gene is located is missing.
In the future, a new genetic technique (called exome sequencing) may also allow this diagnosis to be made without specific consideration or search.

MRI scan
In children with a developmental delay, an MRI scan will often be made to see if there are any specificities in the brain. For a large proportion of children, this MRI scan looks completely normal. In a small proportion of the children, abnormalities are seen, but these abnormalities also occur in children with other syndromes and are not specific to KDM5C syndrome.

Metabolic research
Children with developmental delays often receive blood and urine metabolic tests to see if there is a metabolic disease that explains the developmental delay. For children with KDM5C syndrome, no details are seen in routine research.

EEG
Children with epilepsy often get an EEG to see what type of epilepsy there is. Epileptiform abnormalities are often seen on the EEG. These abnormalities are not characteristic of KDM5C syndrome, but can also be seen in many other syndromes with epilepsy.



How is KDM5C syndrome treated?

No cure

There is no treatment that can cure KDM5C syndrome. The treatment is aimed at stimulating children as well as possible in their development and learning to deal with the problems associated with this syndrome.

Glasses

Some of the children need glasses to see well. Often it concerns glasses with so-called + glasses to be able to see better nearby.

VISIO / Bartimeus
VISIO and Bartimeus are institutions that support children and adults who are visually impaired or blind.

Physiotherapy
A physiotherapist can give parents tips and advice on how to stimulate their child as well as possible to ensure that the development proceeds as optimally as possible.

Speech therapy
A speech therapist can give tips and advice if there are problems with sucking, drinking, chewing or swallowing. The speech therapist can also help to stimulate speech development as well as possible. Talking can also be supported by means of gestures or pictograms. In this way children can learn to express themselves even if they cannot yet use words. Some children benefit from a speech computer.

Occupational therapy
An occupational therapist can give tips and advice on how care and daily activities of a child can go as smoothly as possible. The occupational therapist can also advise on materials that can stimulate the development of a child.

Rehabilitation doctor
A rehabilitation doctor coordinates the various therapies and also advises on aids such as a modified buggy, a wheelchair, arch supports or adapted shoes. It is also possible to go to a modified toddler group via a rehabilitation center and to receive therapy there and to follow education in the same way later.

School
Most children with KDM5C syndrome need extra guidance in learning. Many children are difficult or very difficult to learn. Part of the children can follow regular education with the help of an adapted learning program and extra support. This is according to the minister's plan that all children must go to regular education. Another part of the children eventually go to special education in cluster 2,3 or 4 because they are in smaller classes there and can receive more help and therapy. A part of the children is not learnable and will go to day care.

Orthopedagogue
An orthopedagogue can give parents tips and advice on how to deal with problems such as being angry quickly or making contacts with other children.

Child and adolescent psychiatrist
A child and adolescent psychiatrist can provide advice on how to deal with behavioral problems such as ADHD, aggression or autism. Sometimes it is necessary to give behavioral medication such as methylphenidate for ADHD or risperidone for irritant hypersensitivity.

Treatment of epilepsy
Medication is used to try to prevent epilepsy attacks as much as possible and preferably to ensure that there are no epilepsy attacks at all. Sometimes this

is quite easy with a medicine, but for some of the children it is not that simple and combinations of medicines are needed to prevent the seizures as much as possible or not at all. Different types of medication can be used to control epilepsy. There is no special preferred medicine for this syndrome.
For some of the children it will not be possible to control the seizures with medication. There are also other treatments that can have a good effect on epilepsy, such as a ketogenic diet, a vagus nerve stimulator, or treatment with methyl prednisolone. A combination of these treatments with drugs that suppress epilepsy is also possible.

Treatment of sleeping problems
A fixed *sleeping* ritual and a fixed sleeping pattern can help children to sleep better. The melatonin drug can help you fall asleep better. There are also forms of delayed-release melatonin that can also help you fall asleep again when children wake up at night. Sleeping aids are preferably not given to children because children are used here and cannot live without this medication. Sometimes the drug promethazine is used to help children sleep better. It is always important to exclude that epilepsy is the cause of sleep problems, in case of epilepsy epilepsy treatment is needed.

Clogging of the intestines

The drug macrogol can ensure that the stools remain smooth and soft and stimulates the intestinal wall to remain active. This makes it easier for children to lose their stools. Furthermore, it remains important to ensure that children get enough moisture and fiber and can move as much as possible. Sometimes suppositories are needed to get the stools going.

Antibiotics
Some of the children who often have recurrent infections benefit from a low dose of antibiotics to prevent new infections. For each child, the benefits of giving the antibiotics must be weighed against their disadvantages (antibiotics also kill useful bacteria in the intestines).

Counseling
A social worker or psychologist can give counseling how having this disorder can get a place in daily life. It often takes time for parents to process that their child's expectations for the future look different than expected.

Contact with other parents
By means of a call on the forum of this site you can try to get in touch with other children and their parents / guardians who are also involved in the forum of this site .

What is the prognosis of KDM5C syndrome?
Permanent problems
Children who have a developmental delay due to KDM5C syndrome often continue to have these problems in adulthood. Young adults can often need the help of others to function.

Adults
Because little is known about this disease, not much is known about adults with this condition.
It is therefore difficult to indicate what having KDM5C syndrome means for the future.

Life expectancy
The life expectancy of children and adults with KDM5C syndrome is strongly related to the complaints caused by KDM5C syndrome. For most children, life expectancy will not be different from that of children without this syndrome. Life expectancy can be shortened due to a difficult-to-treat form of epilepsy.

Children get
Adults with KDM5C syndrome can have children. These children have a 50% chance of getting the error in the KDM5C gene themselves. Boys are more likely to suffer from this than girls.

Do siblings also have an increased chance of also getting KDM5C syndrome?
The KDM5C syndrome is caused by an error in the genetic material of the X chromosome. If the mother has a mistake on the X chromosome, siblings have up to 50% chance of getting KDM5C syndrome.
When the defect in the KDM5C gene has occurred in the child itself, then siblings hardly have an increased chance of developing KDM5C syndrome. This could only be the case when one of the parents has the fault in the egg cells or sperm cells, without being in the other body cells. The chance of this is small.
A clinical geneticist can provide more information about this.

Prenatal diagnosis
If it is known which fault in a family has caused the development of KDM5C syndrome, it is possible to perform prenatal diagnosis during pregnancy in the form of a flake test or amniotic puncture to see if this child also has it. Has KDM5C syndrome.
Both procedures have a small risk of miscarriage (0.5% for the floc test and 0.3% for the amniotic puncture). More information about prenatal diagnosis can be found on the website: www.npdn.nl.

If you want to print this document, you can download a pdf version here.

If you also want to share your story, you can: stories can be emailed via info@kinderneurologie.eu and will then be posted on the site as soon as possible. For more information see here

*If you have **photos** that show certain characteristics of this condition and that may be posted here on the website, we would like to hear this.*

Links and references
www.bosk.nl
(association of disabled people and their parents)
www.hersenstichting.nl
(foundation that makes known various brain disorders)
https://www.facebook.com/groups/kdm5c/
(Facebook group of parents with KDM5C syndrome in English)

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