Inform Network Support

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http://www.rarechromo.org/donate Please help us to help you!

Support groups and Facebook groups

SATB2 Gene Trust UK - www.satb2gene.com
American SATB2 Gene Foundation - www.satb2gene.org
Dr Yuri Zarate leads a SATB2-associate syndrome registry with patients from 17 different countries. For more information, visit: www.satb2gene.com
European Foundation for SATB2-associated syndrome - www.satb2europe.org
SATB2 Gene Foundation Australia - www.satb2.org.au
SATB2 Syndrome (2q33.1) and Glass Syndrome - www.facebook.com/groups/185098831860332
SATB2 Syndrome (2q33.1) - UK Parents & Carers - www.facebook.com/groups/1962150980746202
Parent Group. SATB2 Australia (Glass Syndrome, SAS, 2q33.1) www.facebook.com/groups/1938893969766590

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Understanding Chromosome & Gene Disorders

SATB2-associated syndrome (SAS)/Glass syndrome

rarechromo.org

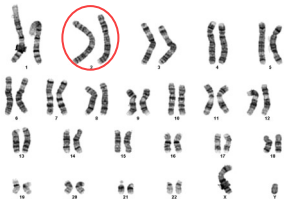
This guide is designed to help families and professionals looking after people affected by *SATB2*-associated syndrome. It contains information about the cause, the ways in which it can affect people and suggestions about the help and management that can benefit people with this condition. It also contains details about support groups and further information that families can access.

What is *SATB2*-associated syndrome?

SATB2-associated syndrome (SAS) is a multisystem neurodevelopmental disorder caused by alterations in the *SATB2* gene. SAS is also sometimes referred to as *SATB2* syndrome, Glass syndrome or 2q33.1 microdeletion syndrome. SAS is characterised by developmental delay/learning (intellectual) disability, limited or absent speech, craniofacial anomalies (such as cleft palate, dental anomalies, a prominent nasal bridge) and behavioural concerns.

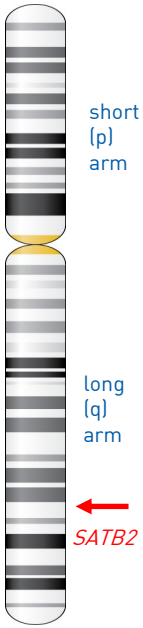
What causes *SATB2*-associated syndrome?

Genes provide the instructions that tell the body how to develop, grow and function. They are made of DNA and are incorporated into organised structures called chromosomes. Chromosomes therefore contain our genetic information. Chromosomes are located inside our cells, the building blocks of our bodies.



Chromosome pairs 1-22, X and Y (male). Chromosome 2 pair circled in red

The *SATB2* gene is located in chromosome 2 in a region called 2q33.1 and is important for the development of the face and the brain. Most of our cells contain 46 chromosomes. We have 22 pairs of 'autosomal' chromosomes, numbered 1 to 22, and two 'sex' chromosomes, two Xs for a genetic female and an X and a Y for a genetic male. We have two copies of chromosome 2 (circled red) and therefore two copies of the *SATB2* gene.



Chromosome 2

SAS occurs when one of the two copies of the *SATB2* gene does not function as expected. Most often this is due to a change (pathogenic variant) within the gene. The second most common cause is loss of an entire copy of the gene (this is called a deletion). The loss of *SATB2* may occur as part of a larger deletion involving other genes in chromosome 2, which may cause additional features. The function of the gene can also be disrupted by a smaller deletion or duplication within the gene (intragenic) or as part of a larger chromosome translocation where the *SATB2* gene is disrupted. A translocation occurs when a chromosome breaks and a portion of it then reattaches in a different chromosomal location. See *Unique*'s guides to Translocations for further information.

Management recommendations

Community paediatricians should oversee care so that development and behaviour can be monitored and the best help in the form of physiotherapy and occupational, speech and behavioural therapies (including medications) can be given early if needed. Consultation with specialists in the field of dentistry is recommended, as well as gastroenterology, cardiology, ophthalmology and neurology, if required.

Children with SAS who have a cleft palate should be under the care of the multidisciplinary cleft team. Expert advice regarding feeding with a cleft is available from the cleft nurse specialists. The best time for the palate to be closed will be decided with the family by the cleft surgeon. Dental, audiology (hearing) and psychology assessment and support is also offered through the cleft team.

Families say ...

"Where do we start? He is our son and the fact that he has some disabilities only makes us feel more protective and loving towards him. He leaps out of bed every morning unlike most teens. Apart from the odd blip in frustration he has a happy disposition and positive attitude. He loves being part of things, doing jobs and feeling a valued member of the proceedings. He has a great memory and is humble when using it, though pleased to be able to help. He is funny and often laughs in the face of adversity. He has a fun sense of humour, but if given an inch can take a mile, so this can cause difficulties with other children."

"As with any parent we share in his achievements and because some of these are such hard work for him, we feel great joy with every step he takes. He has recently started a voluntary job helping at a local café and it is great to see him cycling off to work, so proud to be independent. Although some people can struggle to cope with disability, others have provided him and us with fantastic support and belief in him and his potential." - 16 years

"My son has a very good memory and is good at doing puzzles. I make him feel useful and included in my household chores: he throws out rubbish for me, and can hoover when he is in a good mood. He isn't toilet trained and his fine motor skills are not good, so he needs help with all personal care.

But he is a natural charmer and likes to play tickles with his brothers and sister. Physically he has abnormal dentition, but it doesn't bother him. He looks very handsome. He is very, very special to me, and his big smile on his face every morning makes my day." - 10 years

Medical concerns

Anomalies of the palate and jaw

Many children with SAS have micrognathia (a small lower jaw) and/or an anomaly of the palate (roof of the mouth). Anomalies of the palate range from those that may be invisible to the casual onlooker, such as a high/arched palate, to anomalies such as bifid uvula or cleft palate (where there is a split or fork in the palate, often only the soft palate). A cleft occurs if, early in pregnancy, the separate parts of the developing baby's face (in this case the palatal shelves) don't join as expected. Anomalies of the palate and jaw can contribute to difficulties with feeding, teething, hearing and speech production. Anomalies of the palate cannot be identified on the scans that the mother has during pregnancy but may be found when a baby has a health check after birth. Clefting can be corrected by surgery and special feeding devices or techniques, such as sitting babies up after feeds, can be used to help feed those who are struggling.

Dental anomalies

Dental concerns are very common in children with SAS. These include dental overcrowding, related to micrognathia; teeth that are an unusual shape or size; tooth grinding (bruxism); and teeth being late coming through. It is therefore important that children are under the care of a dentist and have routine assessments.

Seizures

Seizures are uncommon and are seen in a very small proportion of children. They sometimes occur with a temperature.

Skeletal anomalies

Some children may have skeletal anomalies such as tibial or femoral bowing; pectus (chest) deformities; scoliosis, kyphosis or lordosis (curvatures of the spine); or anomalies of the hands/feet. Additionally, some children have osteopenia (low bone mineral density) and broken bones are relatively common in children with SAS.

Brain anomalies

Some children who undergo head magnetic resonance imaging (MRI) are found to have structural brain anomalies. These include enlarged ventricles, abnormal myelination or non-progressive white matter anomalies.

Other organs

There are no structural anomalies of the heart and other organs directly associated with deletion of *SATB2*. However, children with larger deletions that include other genes may have additional features to those in this guide. These features could include cardiac anomalies such as septal defects; genitourinary anomalies such as an inguinal hernia; ectodermal changes such as thin/sparse hair; or changes to vision such as long- (hypermetropia) or short-sightedness (myopia).

Can it be cured?

There is no cure for this disorder as the effects of the genetic change took place during a baby's formation and development. However, knowing this diagnosis means that appropriate monitoring and treatment can be put in place for each child.

Why did this happen?

When children are conceived, their parents' genetic material was copied to produce the egg and sperm that make a new child. The biological copying method is not perfect and occasionally random, rare changes occur in the genetic code of children, which are not seen in the DNA of their parents. These types of change happen naturally and are not due to anything a parent did or did not do. No one is to blame when they occur, and no one is at fault.

In most families the change in the *SATB2* gene occurs out of the blue (*de novo*) in the child. In one case in the medical literature, a parent of two siblings with SAS was found to carry a pathogenic change in the gene in some (but not all) of the cells of their body. Doctors call this mosaicism. The affected parent had no developmental problems or learning difficulties.

In a few families, more than one child had SAS but neither parent was found to carry the genetic change by analysis of their DNA from a blood sample. This suggests some of the mother's egg cells or father's sperm cells carried the genetic variant. This is known as germline (gonadal) mosaicism and is very rare.

Can it happen again?

The possibility of having another child affected by a rare gene disorder depends on the genetic code of the parents. In cases where the parents do not carry the same change in *SATB2* as their child, the chance of having another child with SAS is very low.

In rare cases of germline mosaicism, where the genetic change is only present in some of the mother or father's egg or sperm cells, a person can have more than one child with SAS even though their genetic test, from a blood sample, does not show the genetic change. This genetic change would not, therefore, be detected from this parent's blood test but could still be passed on to future children. If the genetic analysis of the parents of a child with SAS shows they carry the same variant, the possibility of having another child who is affected is much higher. Each family situation is different, and a clinical geneticist can offer specific advice for a particular family.

SATB2 and 2q33.1 microdeletion syndrome

2q33.1 microdeletion syndrome is caused by deletion of a small part of chromosome 2 involving band 2q33.1, including the *SATB2* gene as well as other genes. Children with 2q33.1 syndrome and those with SAS often have similar features. It is likely that some of the features associated with 2q33.1 syndrome

such as cleft palate are due to the loss of *SATB2*, but extra features in those with 2q33.1 microdeletion syndrome compared to SAS are likely to be due to the loss of additional genes in the 2q33.1 region. See *Unique*'s guide to 2q33.1 deletions and other deletions between 2q31 and 2q33 for more information.

Most common features

- Learning (intellectual) disability or slow learning
- Developmental delay
- Absent or severely delayed speech
- Anomalies of the palate
- Dental anomalies/crowding
- Characteristic facial features such as a prominent nasal bridge, bulbous tip to the nose and a small chin
- Hypotonia (low muscle tone) and feeding difficulties in infancy
- Behavioural concerns such as hyperactivity, aggressive outbursts or autistic behaviour/autism spectrum disorder (ASD)
- Growth restriction in infancy

Other possible features

- Skeletal anomalies (low bone mineral density)
- Seizures
- Brain anomalies
- Joint hypermobility

Development

Growth

Some babies are average in weight at birth and continue to grow along their centile lines but many have growth restriction in infancy, often because of poor feeding - this is more common in children with larger deletions including other genes. Most of these babies go on to grow well but remain relatively thin. Some older *Unique* children with SAS are noted to be tall and slender.

Feeding

Many babies may have initial difficulty with feeding due to features such as cleft palate and low muscle tone. The low tone usually resolves with time and most children gain weight and grow well. Dribbling can be a problem for some, but this can be helped by medicines to reduce saliva production. Many babies benefit from the use of specialised feeding devices or techniques. Very occasionally, a feeding tube is required. A feeding or speech therapist will help to find ways to feed children with feeding difficulties.

Sitting, moving and walking

Many babies will have low muscle tone which can make a baby or child floppy to handle and make achieving mobility milestones more difficult. Their joints may also be excessively flexible (hypermobile). Children are usually late in becoming mobile, but most start walking independently by the age of 2 years, although for some this may take much longer. Physiotherapy often proves beneficial.

Speech and communication

Children find it difficult to co-ordinate movement of their lips, jaw and tongue to make the sounds of speech (apraxia of speech). Some children learn single words, but many do not develop speech. Instead, they communicate by other means, such as sign language, gestures and vocal noises. Many children benefit from the use of technology to aid their communication, and many children can learn to communicate their needs and thoughts using Makaton or modified sign language.

Ability to learn

Most children need considerable support with their learning and benefit from attending a special school where the right support can be given, and non-academic and daily living skills focused on. Several *Unique* parents commented on their child's good memory and interest in puzzles. Supervision may be needed even for adults.

Behaviour

Children usually have a happy disposition and are seen to be very sociable and even over-friendly. Autistic traits are common and many children have a formal ASD diagnosis. Hyperactivity may be seen, and occasionally aggressive behaviour - more often in older individuals. Advice should be sought where there are particular concerns. For instance, an occupational therapist may be able to help with some behavioural issues by giving your child tools to deal with their sensitivities. Joining a social skills group may help a child with social difficulties to learn and practise important social skills.

Sleep disturbances have been frequently noticed by parents and can be severe enough to need medication.