

What causes KBG syndrome?

KBG syndrome is caused by one copy of the *ANKRD11* gene not functioning properly. This may be due to a change (mutation) within the gene which disrupts its function, or to the loss (deletion) of the gene or part of it. The other copy is unaffected.

Why did this happen?

When children are conceived their parents' genetic material is copied in the egg and sperm that makes a new child. The biological copying method is not perfect and occasionally random, rare changes occur in the genetic code of children that are not seen in the DNA of their parents.

KBG syndrome occurs when one of these random, rare changes affects the *ANKRD11* gene on chromosome 16. These types of change happen naturally in all species - humans, plants and animals - and are not due to your lifestyle or anything you did.



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 most families, the genetic change has happened for the first time in the child with KBG syndrome. We call this a 'de novo' change. In this situation, when the parents are unaffected, the chances of having another child with the same condition are very low (usually less than 1%). If a parent has KBG syndrome, the chances of passing the condition on to a child are much higher at 50%, or 1 chance in 2, as the parent could either pass on their altered copy of the gene or the unaffected copy. This inheritance pattern is called Autosomal Dominant (because the change is on an autosomal chromosome and an outcome can be seen if only one copy of the gene is altered). Each family situation is different and a clinical geneticist or genetic counsellor can give specific advice for your family.

Families say ...

"My little boy is special to me because every day he surprises me. We strive for progress and not perfection in our house. It's the little things he does that makes me so proud, I am truly blessed to be his mother. To raise such a special little boy really motivates me to be the best version of myself. Having him has contributed to my family and myself by giving us a purpose. We all try to help him have the best quality of life which has made us a stronger family unit. We couldn't imagine life without him." - age 2½

"Jane is very special to me. I knew from the moment she was born that there was something unique about her. She has always had such a peaceful demeanor about her. She brings a joy and light into everyone's life that she meets. One thing that makes Jane so special is that she has no appetite. She never has shown any signs of hunger even as an infant. She has taught me that each of us have our own way of doing things and we all bring something special to life. I have learned to accept new challenges and to embrace life at a different speed than most other moms I know. Because of Jane, I have met people whom I would have never met otherwise. I have learned to celebrate the little things in life that we so often overlook. She has taught me patience and compassion. Because of her I have been able to empathize with others and to honestly say I know how they feel. My life is so richly blessed by Jane and I am grateful every day that she is my baby girl." - age 2½

Inform Network Support

Rare Chromosome Disorder Support Group,

The Stables, Station Road West, Oxted, Surrey RH8 9EE, UK

Tel: +44(0)1883 723356

info@rarechromo.org | www.rarechromo.org

This guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change. Unique does its best to keep abreast of changing information and to review its published guides as needed. This guide was compiled by Dr Tazeen Ashraf, Dr Karen Low and Dr Natalie Canham, Clinical Geneticists in the UK.

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Understanding Chromosome & Gene Disorders

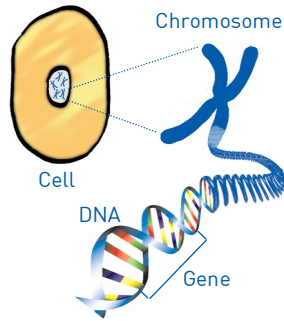
ANKRD11 and KBG syndrome

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What is KBG syndrome?

KBG syndrome was first described in 1975, and its name is derived from the initials of the first three patients reported with the condition. People with KBG syndrome have a characteristic (and sometimes subtle) facial appearance, very large permanent teeth, and variable degrees of developmental delay, learning difficulties and behavioural problems. As the appearance can be subtle, the diagnosis may not be made until the permanent teeth have come through. Other features seen in some affected individuals include conductive hearing loss, undescended testes in boys, seizures, skeletal abnormalities and short stature.



KBG syndrome is caused by changes (mutations) in or a deletion of the *ANKRD11* gene on chromosome 16 (band q24.3). Most affected people are the first person in their family to carry the gene change, but a small proportion have inherited it from a parent, who is likely to have features of KBG syndrome. The condition affects boys and girls, and there are both mildly and more significantly affected individuals of both sexes. However, there appear to be more reports of affected males than females at a ratio of around 3:2 but the reason for this is unclear.

Most people have:

- A degree of developmental delay and some element of unusual behaviour
- Large permanent upper middle teeth (macrodonia of upper central incisors)
- Characteristic facial appearance: triangular face, wide-spaced eyes and thick eyebrows, sometimes joining in the centre (synophrys)
- Short fingers (brachydactyly) with curved 5th finger (clinodactyly)

How common is KBG syndrome?

It is extremely rare and thought to affect several hundred people worldwide. It is likely that many people are not diagnosed because many of the features can be mild, including learning disabilities, in those with a change (mutation) in *ANKRD11*.

Medical concerns

The amount of medical problems a person with KBG syndrome will have is extremely variable and impossible to predict. Below are some of the more common problems that could be observed in affected individuals:

Seizures Around 20-40% of people are reported as having seizures, of varying types. Seizures typically respond to the usual anti-epileptic treatments.

Hearing A significant proportion of people have recurrent otitis media or glue ear (a build-up of fluid in the ear), which can cause conductive hearing loss, where sounds are unable to pass into the inner ear. Many children have required multiple grommet insertions to relieve pressure inside the ear, and some have still required hearing aids. Hearing should be carefully and regularly checked during the first few years. Many children have speech delay which may be linked to their hearing problems.

Eyesight People with KBG syndrome are more likely to have vision problems such as astigmatism (the front of the eye is not perfectly rounded, causing blurry vision), and short or long-sightedness. Squint, where the eyes do not look in the same direction, can occasionally be a feature. Treatment can include patching, exercises, glasses, and surgery to bring the eyes into line.

Undescended testes Many boys with KBG syndrome are born with testicles that have not completed their journey from the tummy (abdomen) to the sack (scrotum). In some boys, the testes descend in due course on their own, but if they do not, they can be brought down and fixed in the scrotum with a simple surgical operation.

Skeletal Some people with KBG syndrome have an unusual structure of their spinal bones which can give rise to an increased curvature of the spine (scoliosis). Babies may experience a delayed closure of the soft spot on their head (anterior fontanelle). Many people with KBG syndrome have short fingers (brachydactyly) with a curvature of the 5th fingers (clinodactyly).

Teeth As well as large front teeth, there can be a variety of other dental problems. Enamel defects are frequently seen, and careful brushing is very important. It is important for children with KBG syndrome to have regular dental check-ups.

Feeding Many babies have feeding difficulties and some require short-term nasogastric tube feeding to supplement oral feeds. It is Unique's experience that lack of interest in feeding can be significant and long-lasting. A very small number of children have required longer term tube feeding.

Development

■ **Physical development**
People with KBG syndrome do learn to walk alone, but this is frequently delayed.

■ **Learning**
Children with KBG syndrome typically need extra help in school, though most go to a mainstream primary school. The extra demands of mainstream secondary school may prove too challenging, and children may transfer to special schooling or remain in mainstream schools with Educational Health Care Plans (EHCP). Those with chromosome deletions may have more significant problems, which are probably related to other genes which are also deleted. There have been reports of children with small *ANKRD11* deletions or mutations who have no learning or development difficulties.

■ **Behaviour**
People with KBG syndrome often have behavioural issues such as autism, ADHD or anxiety.

■ **Speech**
The vast majority of people with KBG syndrome learn to speak normally, but speech delay is very common. Hearing loss and subtle palate problems can worsen speech delay.

■ **Using their hands**
Fine motor development is frequently delayed, but typically full function is attained.

Growth

Babies with KBG are usually a normal weight at birth, but grow more slowly in childhood. Typically children are around the 9-25th centile for height on their age-appropriate growth chart but there are reports of people with KBG syndrome with average and above average height.

Management recommendations

- Regular dental check-ups
- Regular hearing reviews to age 5 (even if earlier reviews are normal)
- Eyesight (ophthalmology) review
- Check position of testes in boys
- Consider a palate review (particularly if there are feeding difficulties or speech problems)
- Consider a cardiac review
- Consider a skeletal review

