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.
In most families the DNA change in *ANKRD11* occurs out of the blue (de novo). In a few families, one parent may have the same genetic change as their child, but this is 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. Where parents do not carry the same *ANKRD11* change as their child, or any other change that could affect *ANKRD11*, the chances of having another child are almost certainly no higher than for anyone else in the population. If the genetic analysis of the parents of a child with KBG syndrome shows that they carry the same change in the *ANKRD11* gene, the chances of it happening again are much higher, and could be as high as 50:50 in any pregnancy. Each family situation is different and a clinical geneticist or genetic counsellor can give you 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

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Understanding chromosome disorders Unique

ANKRD11 and KBG syndrome

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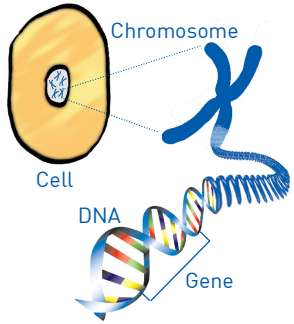
What is KBG syndrome?



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 have a characteristic (though subtle) facial appearance, very large permanent teeth, and variable degrees of developmental delay and learning difficulty. As the appearance is subtle, the diagnosis may not be made until the permanent teeth come through. Other features seen in some affected individuals include short stature, epilepsy, undescended testes, rib and spine anomalies and conductive hearing loss usually caused by glue ear.

KBG syndrome is caused by changes (mutations) in or a deletion of the *ANKRD11* gene on chromosome 16q24.3. 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 severely affected individuals of both sexes. However, there appear to be more reports of affected males, and this may be linked to sex hormones, with which the *ANKRD11* gene interacts.

Most people have:

- A degree of developmental delay
- Large permanent upper middle teeth
- Characteristic facial appearance
- Curved 5th finger (clinodactyly)
- Undescended testicles in boys

How common is KBG syndrome?

It is probably rare, but no-one knows exactly. 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

People with deletions including *ANKRD11* may well have other genes within the deletion, and this can increase the likelihood of medical problems over those with changes (mutations) in the gene.

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 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 found that they 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.

Eyesight People with KBG 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 Most 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 in a short surgical operation.

Spine Curvature of the spine. Some people with KBG have an unusual structure to their vertebrae (spinal bones) which may give rise to scoliosis.

Teeth As well as large front teeth, the molars may also be large, which can cause orthodontic problems, as the teeth are too large for the jaw. Enamel defects are very frequently seen, and careful brushing is very important.

Feeding It is Unique's experience that lack of interest in feeding can be significant and long-lasting.

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 many transfer to special schooling at this point. 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 a small *ANKRD11* deletion and no learning or development difficulties.

Behaviour

People with a deletion of *ANKRD11* frequently have autistic features. This is less common in those with a mutation in the gene.

Speech

The vast majority of people with KBG syndrome learn to speak normally, but speech delay is very common. Hearing loss 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 around half grow slowly, and are unusually short for their age as children and adults. There are however people with KBG of average and above average height.

Management recommendations

- Regular dental check-ups
- Regular hearing reviews to age 5 even if earlier reviews normal
- Check position of testes in boys
- Chest X-ray to check ribs and spine
- Eyesight (ophthalmology) review.