Understanding chromosome disorders

Unique

Duplications of proximal 16q

rarechromo.org

Sources and References

The information in this leaflet is drawn partly from the published medical literature. The first-named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed. A full literature list appears on page 7.

The leaflet also draws on *Unique*'s database. When this leaflet was written, *Unique* had 32 members with a duplication of 16q, of whom 10 had a pure duplication of 16q without involvement of other chromosome material. One member had a pure duplication of proximal 16q.

A chromosome 16 duplication is a rare genetic condition in which there is an extra copy of part of the genetic material that makes up one of the body's 46 chromosomes. Each chromosome has a short (p) arm and a long (q) arm. The long q arm is at the bottom in the diagram below. A 16q duplication means that some material from the long arm has been duplicated.

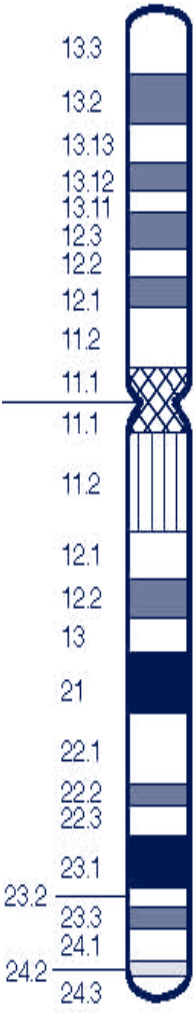
Like most other chromosome disorders, this can increase the risk of birth defects, developmental delay and learning difficulties. However, the problems that can develop depend very much on what genetic material has been duplicated. This leaflet tells you what is known about the effects of a 16q duplication from reports in the medical literature and family members of *Unique*.

Looking at chromosomes

Chromosomes can be stained so that each one has a distinctive pattern of light and dark bands when viewed at about 1000 times life size under a light microscope. You can see these bands in the diagram on the right. The bands are numbered outwards starting from the point where the short and long arms meet (the **centromere**). Each chromosome arm is divided into major areas 1, 2 and 3 and each of these is subdivided so that each band has a unique number within the arm. A low number such as q11 is close to the centromere and the part of the arm that is fairly close to the centromere is called the **proximal** part. A higher number such as q24 is closer to the end of the chromosome, in the part referred to as **distal**.

Your geneticist or genetic counsellor will tell you more about how much chromosome material has been duplicated. You will almost certainly be given a **karyotype**, a shorthand notation for your child's chromosome make-up, which will show the breakpoints in the chromosome.

Comparing your child's karyotype with others in the medical literature and in *Unique* will help to build up a picture of what to expect. But there will still be differences, sometimes quite marked, between your child and others with apparently similar duplications. It is very important to see your child as an individual and not to make direct comparisons with others with the same karyotype. After all, each of us is unique.



Chromosome 16

Proximal duplications between 16q11 and 16q13

Most common features

- Developmental delay
- Learning difficulties and speech delay
- Minor anomalies of the hands and/or the feet
- Abnormal tooth development, most often small teeth
- Difficulties with attention and/or behaviour
- Usually healthy with no major birth defects

Growth

There is information about growth and or body build in 10 people, including six children and four adults. Among the children, three were of normal height at ages 3, 4 and nine years and two children were short for their age at four and five years old. Among the adults, three were short or very short, a 34-year-old woman just four foot six (145cm) tall. One adult, with a large duplication between 16q12.1 and 16q13, was of normal height.

In terms of body build, two adults were described as either stocky or mildly obese and three children aged between five and nine years were also plump or overweight.

> “ He’s the right height for his age, but plump round the tummy and chest as he does not exercise much. ”

Appearance

There may be little sign in the facial appearance of a baby, child or adult of the underlying disorder. Doctors may notice what are known as ‘dysmorphic features’ which can mean that a child looks more like others with a proximal 16q duplication than like his parents. A fine upper lip and occasionally a flat groove between the upper lip and nose have been observed most commonly, as have slanted eyes, more often slanting upwards than down.

Unusual features and clinical concerns

Hands and feet

Minor, non-functional anomalies of the hands and feet are fairly common in people with a chromosome disorder. In this group, most people were not described as having unusual hands or feet. Individuals who were affected had quite different unusual hand features. A mother and son each had short, stubby thumbs; two unrelated people had incurving fifth fingers and another had incurving third, fourth and fifth fingers. One adult had small hands with short, thick fingers; another had bent end joints on the fingers but extremely flexible knuckle joints.

In two people, hands and feet were unusual in a similar way – one adult had small hands and feet, another had bent toes and fingers. Fingers and toes that are bent at the joints may be treated by splinting or surgery. Another child had prominent heels. It is not necessary to treat prominent heels or small feet. One child had slightly flat feet; children usually grow out of flat feet, but if there is any concern, they should be assessed and if necessary treated with exercises or suitable footwear. Another child

had unusually angled feet, which may be treated with stretching, physiotherapy, splinting or surgery, depending on the type and severity (Barber 2006; Spillane 2006; Stratakis 2000; Romain 1984; *Unique*).

Teeth

Two children and one adult had small teeth that might be widely spaced. Another child had 'good, strong' teeth but some permanent teeth came through before the milk teeth fell out (Barber 2006; Spillane 2006; Stratakis 2000; *Unique*).

Hernias

Two types of hernia have been reported. Two children had an inguinal hernia (in the groin), where part of the bowel loops through an opening in the inguinal canal. An inguinal hernia needs surgery to prevent the possibility that the loop of bowel might get trapped. Two children had an umbilical hernia (near the navel), caused by a weakness on the abdominal wall. An umbilical hernia may sometimes correct itself or surgery may be needed to strengthen the area of the hernia (Barber 2006; Stratakis 2000; *Unique*).

Genitals and reproductive system

Children with chromosome disorders, in particular boys, are more liable to be born with minor genital anomalies than other children. Three children in this group had a minor anomaly, each one different. One boy was born with one testicle not yet descended into the scrotum. Treatment for undescended testicles depends on the suspected cause but whatever the cause, treatment is usually needed if the testicles have not descended naturally from the abdomen by early childhood. One boy had a hydrocele (a collection of fluid in the scrotum). If a hydrocele is found in a baby at birth, it is usually fixed soon afterwards by a short surgical operation in which the fluid is removed from the hydrocele and the passage between the abdomen and scrotum is sealed off. An unborn baby girl was found to have faulty development of the ovaries (Barber 2006; Spillane 2006; Trimborn 2006).

Eyesight

Two children and an adult had long sight and the two children also had a squint (strabismus). Long sight is usually corrected by glasses. Treatment of strabismus depends on the cause but can include patching the stronger eye, exercises, glasses to correct a refractive error such as long sight and surgery to realign the muscles that hold the eye in place (Barber 2006; Stratakis 2000).

Heart conditions

The great majority of children and adults had a normal, healthy heart. Heart conditions were found in one child and one adult but the conditions were quite different from each other. In one child, the aortic isthmus (a naturally narrow segment of the aorta between the part that rises from the heart and supplies blood to the head and the part that descends to supply blood to the rest of the body) was narrowed. In one adult, the left upper chamber of the heart (atrium) was enlarged but the heart was otherwise normal and healthy (Barber, 2006; Stratakis 2000).

Other clinical problems

Uneven breast size An adult with a duplication of 16q13 had one breast that was very much larger than the other and this persisted, despite breast reduction by surgery.

It is not known whether this condition relates to her 16q duplication or not (Stratakis 2000).

Blood vessels An unusual formation of the arteria thyroidea ima was noticed in an unborn baby with a duplication of 16q11.2q13 (Trimborn 2006). This is a blood vessel that leads to the thyroid gland and is present in embryonic life but only persists in a few people (1-2 per cent) after birth.

Abnormal hip development One baby was born with hip subluxation, a condition in which there is incomplete contact between the surfaces of the bones in the joints, so the hips can easily dislocate (Fryns 1990). Abnormal hip development is fairly common in children with chromosome disorders and treatment depends on individual assessment but can include postural management programmes, splinting and surgery.

Sitting, moving: gross motor skills

Some delay in reaching childhood developmental milestones has been seen in all affected children and adults, although the amount of delay is generally only moderate. After a slow start in rolling, sitting and crawling, children were able to walk between 18 and 25 months. Some children, but not all, had low muscle tone (hypotonia), which makes the muscles feel floppy and the joints often hypermobile. Babies with hypotonia usually need extra stimulation to learn to use their muscles in the right way. Most babies and children with developmental delay or hypotonia are referred to a physiotherapist for assessment and regular treatment with exercises and activities. Depending on the severity, aids may be needed to help with mobility, such as orthotic supports, standing and walking frames.

One adult of 28 years has been reported with spastic quadriplegia, in which the muscles of both arms and legs are stiff, making movement difficult (Engelen 1999).

> “ The first sign that anything was wrong was that he could not do forearm push-ups at six months, he was late to sit up unaided, did not crawl until he was taught to and held his right arm tucked into his body. Over the years his confidence when walking has increased but now, aged nine, he still walks carefully. Because of his low muscle tone, he naturally walks on his insteps, so he wears foot-to-knee splints to improve his leg position. ”

Learning

Children with a proximal 16q duplication will usually need support with their learning, but the extent is varied. The range of learning disability is from mild to severe, with most children having moderate difficulties and attending a special school. Among some children with a moderate learning difficulty, reading and writing skills did emerge.

> “ His school is using his very good visual memory as an aid to teaching. ”

Speech and communication

Speech and language appear to be delayed in line with a child’s learning disability and for some children a delay in talking was the first sign that anything was wrong. The evidence from both the medical literature and *Unique* is that some speech does generally develop. Understanding appears to be more advanced, especially in a familiar context.

Speech therapy is helpful and some children have benefited from learning a sign language or a system such as Makaton that bridges sign language and speech.

Behaviour and attention

Some degree of difficulty with behaviour, attention or activity level seems to be common, but this may be because most of the reports come from medical journals. One adult was described as having a pleasant 'party-like' personality, and a child has been described as 'good-natured'.

Challenging behaviour or problems with aggression have occurred in quite young children of pre-school and early school age. Support for behaviour difficulties should be available to families via their developmental paediatrician, primary caregiver (GP) or their local mental health service.

Hyperactivity/ attention deficit The way attention deficit and hyperactivity are managed depends on the underlying cause (the chromosome disorder) as well as any additional causes (such as difficulties with hearing or emotional upset). Behaviour management using clear, firm and consistently reinforced guidelines should be offered with full support to the family. Medication may prove helpful in enabling children to concentrate for longer, to complete tasks and learn more (Barber 2006; Spillane 2006; Engelen 1999; Verma 1997; Fryns 1990; Romain 1984).

Outlook

The outlook depends mostly on how much the chromosome disorder affects an individual child or adult. For guidance, however, adults have been described, mostly living in a supported or a semi-sheltered environment, but in some cases living independently. At least two adults, twin brothers with a 16q11.2q12.1 duplication, worked in a supported environment (Barber 2006; Engelen 1999; Verma 1997; Romain 1984).

Can this happen again?

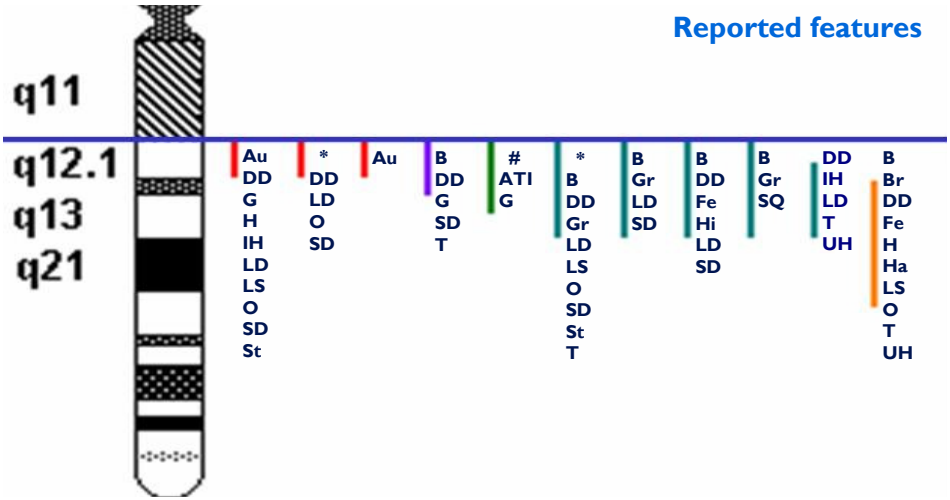
The possibility that a couple will have another pregnancy affected by a 16q duplication depends on their chromosomes. If both parents have normal chromosomes, the 16q duplication in the child has in all probability occurred as a chance event, in which case the karyotype will be marked *de novo* or *dn*. It is then very unlikely to happen again. If a test of the parents' chromosomes shows that either has a chromosome rearrangement involving 16q, the chances of another affected pregnancy are much higher.

In quite a few families, a 16q duplication has been passed down directly from one parent (either mother or father) to one or more children with no apparent effect on fertility. In these families, the risk of another child having the family 16q duplication can be as high as 50 per cent.

Will a child with a 16q duplication have similarly affected children?

Adults with proximal 16q duplications may form close relationships and want to have children. In each pregnancy, someone with the duplication has a 50 per cent risk of passing it on and a 50 per cent chance of having a child without the duplication. Their ability to look after a child is very likely to be closely related to their own degree of learning difficulty.

Reported features



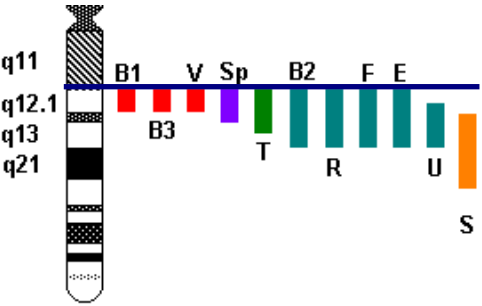
Au Autism/ autistic features
ATI Arteria thyroidea ima (*unusual blood vessel, see text*)
B Behaviour problems
Br Uneven breast size
DD Developmental delay
Fe Foot malformation
G Unusual genital/reproductive feature
Gr Growth delay
H Heart anomaly
Ha Unusual hand feature
Hi Hips easily dislocated
IH Inguinal hernia (*in groin*)
LD Learning difficulty
LS Long sight
O Overweight
SD Speech delay
SQ Spastic quadriplegia
St Strabismus (*squint*)
T Unusual dental development
UH Umbilical hernia (*near navel*)

See text for fuller explanations

* *More than one family member affected; features may vary between family members*

*Unborn baby*

Reported cases



The region of 16q near the centromere known as 16q11 contains only genetically inactive material. The blue line marks the upper limit of chromosome material on 16q believed to affect development. Some individuals and families also had duplications of material above the blue line but duplications from this region are not expected to have any effect. Duplications with an effect probably only start from band 16q12.1.

16q12.1 only

B1 = Case 1 from Cytogenetic & Genome Research 114: 351-8 (2006) Barber et al

B3 = Family 2 from Cytogenetic & Genome Research 114: 351-8 (2006) Barber et al

V = Clinical Genetics 52: 446-7 (1997) Verma et al

16q12.1 and 16q12.2

Sp = Journal of Medical Genetics Supplement 1 S104 (2006) Spillane et al

16q12.1, 16q12.2 and half 16q13

T = Prenatal Diagnosis 26: 273-6 (2006) Trimborn et al

16q12.1, 16q12.2 and 16q13

B2 = Family 3 from Cytogenetic & Genome Research 114: 351-8 (2006) Barber et al

R = American Journal of Medical Genetics 19: 507-513 (1984) Romain et al

F = Annales de Génétique 33 (1) 46-48 (1990) Fryns et al

E = Annales de Génétique 42 (2) 101-4 (1999) Engelen et al

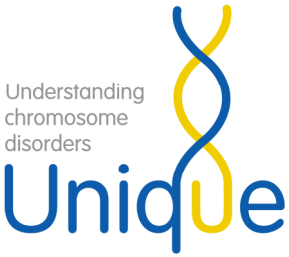
Probably most of 16q12.1, 16q12.2 and 16q13

U = *Unique*

16q12.2, 16q13, 16q21 and proximal 16q22.1

S = Journal of Clinical Endocrinology & Metabolism 85 (9) 3396-3401 (2000) Stratakis et al

Support and Information



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