

# 7q11.23 duplication syndrome



## Sources

The information in this guide 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 (<http://www.ncbi.nlm.nih.gov/pubmed/>). If you wish, you can obtain most articles from Unique. In addition, this leaflet draws on information from a survey of members of Unique conducted in 2010, referenced Unique. When this leaflet was updated in February 2013, Unique had 21 members with a pure 7q11.23 duplication (no other chromosome is involved). These members range in age from a toddler to an adult aged 20 years. When this guide was updated in 2020, Unique had 122 members with a 7q11.23 duplication, three of whom were known to have additional genetic changes.

## 7q11.23 duplication syndrome

A 7q11.23 duplication means that the cells of the body have a small amount of additional genetic material from one of their 46 chromosomes – chromosome 7. For healthy development, chromosomes should contain just the expected amount of genetic material (DNA) – not too much and not too little. Like most other chromosome disorders, having an extra part of chromosome 7 may affect the development and intellectual abilities of a child, although there is considerable variability in these and other individual features that are observed.

## Background on Chromosomes

Chromosomes are genetic structures found in most cells of our body. Each chromosome contains hundreds to thousands of genes. Genes can be thought of as individual instruction booklets (or recipes) that contain all the genetic information that instructs our bodies how to grow, develop and function.

Chromosomes (and genes) usually come in pairs with one half of each chromosome pair being inherited from each parent. We have 23 pairs of chromosomes giving a total of 46 individual chromosomes. Of these 46 chromosomes, two are the sex chromosomes that determine whether we are male or female. Females have two X chromosomes and males have one X chromosome and one Y chromosome. The remaining 44 chromosomes are grouped in 22 pairs, numbered 1 to 22. Each chromosome has a short (**p**) arm (shown at the top of the diagram on page 3) and a long (**q**) arm (the bottom part of the chromosome on page 3).

## Chromosome Duplications

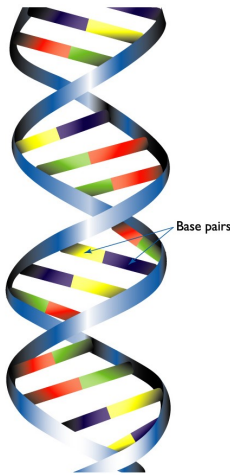
A sperm cell from the father and an egg cell from the mother each carries one copy of each chromosome. When they join together they form a single cell that carries two copies of each chromosome. This cell must make many copies of itself (and all the chromosomes and genetic material) in order to make the trillions of cells that form during human growth and development. Sometimes during the formation of the egg or sperm cells or during this complicated copying and replication process, parts of a chromosome can break off or become rearranged.

People with a 7q11.23 duplication have one intact chromosome 7, but the other copy of chromosome 7 has an extra piece of the long q arm. Therefore it is believed that most of the clinical features associated with 7q11.23 duplications are probably caused by having three copies (instead of the usual two) of a number of genes. We are still learning about the specific roles of the genes in this region (see [Ongoing Research into chromosome 7q11.23](#) on page 19).

## Looking at 7q11.23

Chromosomes can't be seen with the naked eye but if they are stained and magnified under a light microscope it is possible to see that each one has a distinctive pattern of light and dark bands that look like horizontal stripes under a microscope, a bit like a bar code. In the diagram of chromosome 7 on the right you can see the bands are numbered outwards on each arm starting from where the two arms meet (this is known as the centromere). A low number such as 11 is close to the centromere.

Band 7q11.23 is shaded pink in the image opposite. The part duplicated in 7q11.23 duplication syndrome contains about 1.4 million base pairs (1.4 Mb). Base pairs are the building blocks of DNA as shown in the diagram below, they appear diagrammatically much like rungs of a ladder. This may sound like a lot of DNA, but Chromosome 7 has roughly 158 million base pairs in total.

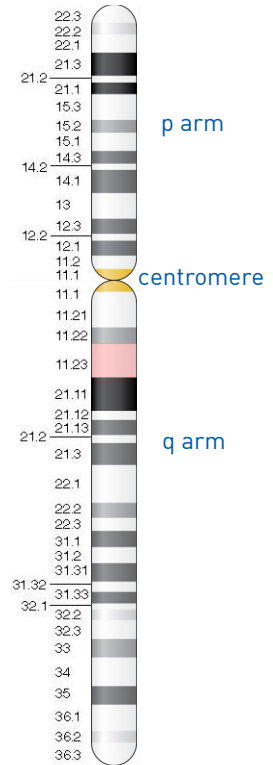


bp = base pair  
Mb = megabases  
(1 million base pairs)

The extra piece of genetic material on chromosome 7 is too small to be seen using a microscope. So a basic chromosome staining analysis (such as karyotyping) is unlikely to identify this duplication.

The duplication can usually be found using more recently developed DNA technology, in particular a technique such as array-CGH (comparative genomic hybridisation) or microarray. This technique identifies gains and losses of small amounts of DNA throughout each chromosome.

Not everybody with a 7q11.23 has exactly the same amount of duplicated DNA. Array technology can show quite precisely how much DNA has been duplicated and which of the 25 to 30 genes found in band 7q11.23 have been duplicated (these genes are listed in the diagram on page 19).



People who have extra material on a chromosome are said to have a **duplication** but when the amount of material is so small that it can't be seen under a microscope, it is called a **microduplication**. Specific 7q11.23 microduplications are often referred to as **7q11.23 duplication syndrome**. It is also possible to have a different microduplication of DNA within 7q11.23 that is completely different and does not overlap at all with the 7q11.23 duplication syndrome microduplication. This guide presents information relating only to 7q11.23 duplication syndrome microduplications.

## 7q11.23 and Williams syndrome

People who have lost this segment of chromosome 7 have a syndrome called Williams (or Williams-Beuren) syndrome. Williams syndrome is caused by a deletion of the same piece of chromosome that is duplicated in 7q11.23 duplication syndrome.

## Results of the chromosome test

Your geneticist or genetic counsellor will be able to tell you more about the specific piece of chromosome 7 that has been duplicated in your child (and perhaps yourself or your partner). With a 7q11.23 duplication, the results are likely to read something like one of the following examples:

### 46,XY,dup(7)(q11.23q11.23)

46 The total number of chromosomes in your child's (or your) cells  
XY The two sex chromosomes, XY for males; XX for females  
dup A duplication of genetic material was identified  
(7) The duplication is from chromosome 7  
(q11.23q11.23) There are two breakpoints in the chromosome, both in band 7q11.23 indicating a small duplication

In addition to, or instead of the information shown above (known as a karyotype) you may be given the results of molecular analysis such as FISH (fluorescence in situ hybridisation) or array-CGH for your child. In this case the results are likely to read something like the following examples:

### 46,XX,ish dup (7)(q11.23q11.23)(RP11-805G2++)dn

46 The total number of chromosomes in your child's (or your) cells  
XX The two sex chromosomes, XY for males; XX for females  
ish The analysis was by fluorescence *in situ* hybridisation (FISH)  
dup A duplication of genetic material was identified  
(7) The duplication is from chromosome 7  
(q11.23q11.23) There are two breakpoints in the chromosome, both in band 7q11.23 indicating a small duplication  
(RP11-805G2++) A DNA fragment of interest known as RP11-805G2 has been found in two copies (on one chromosome) instead of one ++  
dn The duplication occurred *de novo* (as a 'new event'). The parents' chromosomes have been checked and no duplication or other chromosome change has been found. The duplication is very unlikely to have been inherited and has almost certainly occurred for the first time in this child

### arr cgh (7)(q11.23q11.23)(72744455-74142672 )x3 [hg19]

arr cgh The analysis was by array-CGH  
(7) Chromosome 7 has a genetic change  
(q11.23q11.23) The change is between two points on the chromosome, both are in band q11.23 indicating a small duplication  
(72744455-74142672 ) There has been a change identified between base pairs 72744455 (around 72.7 Mb) and 74142672 (around 74.1 Mb). This means about 1.4 Mb of DNA is involved.  
X3 3 copies of this piece of DNA have been identified. Two copies are expected since we have two copies of chromosome 7. This shows a duplication has occurred.  
hg19 This is the reference DNA sequence that the base pair numbers refer to, in this case human genome build 19. Information about the reference human genome sequence is continually updated and new "builds" of the sequence are made. This means base pair numbers are continually adjusted so it is important to note which build your genetic test results refer to.

## Most common features

When only small numbers of people have been identified, we can't yet be certain what the full range of possible effects of the duplication are. In the children who are affected, the features that are most notable and most common are:

- Speech and language delay or disorder
- Learning difficulties. Some children (about 20%) have been identified as having border line intellectual abilities and others (about 18%) have been diagnosed with intellectual disability (ID), but the majority of children reported so far have low to high average intellectual abilities
- Normal growth (although some individuals have short stature and some have been found to have growth hormone deficiency)
- Behavioural difficulties are common and include anxiety disorders (a social anxiety disorder is often identified), other diagnoses include selective mutism, attention deficit hyperactivity disorder (ADHD), oppositional disorders, physical aggression, and autism spectrum disorder (ASD) or ASD like behaviour
- Dilation of the aorta (the body's main artery)
- Birth defects are not often reported. A small number of babies may be born with a split in the roof of the mouth or lip (cleft palate or lip)
- Children are generally healthy although a minority have seizures
- Subtle facial features (a large head (macrocephaly) has been described in about half of people reported with 7q11.23 duplication syndrome)

(For further details in published scientific literature, see Morris 2015 and Mervis 2015)

## How much do we know?

Comparing different children and adults with 7q11.23 duplication syndrome shows that some effects seem to be broadly similar. This information guide tells you what is known about those effects. Comparing your child's diagnosis with others, both in the medical literature and within Unique, can help to build up a general picture of what to expect. But there will still be differences, sometimes quite marked, between your child and others with an apparently similar chromosome diagnosis. It is



important to see your child as an individual and not to make direct comparisons with others with the same diagnosis or syndrome name. A child's other genes, environment and unique personality help to determine their future development, needs and achievements.

## Are there people with a 7q11.23 duplication who are healthy and have developed normally?

Yes, there certainly are. In some families, either the mother or the father has the same 7q11.23 duplication as the child and appears to be entirely unaffected by it. However, careful examination for possible subtle language difficulties have shown that most, if not all carriers will have experienced some language difficulties at some point during their lives (Mervis 2015). This makes it difficult to be certain what the complete effects of having a 7q11.23 duplication are (Kriek 2006; Berg 2007; Van der Aa 2009; Velleman 2011). Recent studies have identified about a quarter of parents as having passed on the duplication to their child (Morris 2015).

## How common are duplications of 7q11.23?

Deletions of 7q11.23 occur at a frequency of around 1 in 7,500 (Morris Gene Reviews) and it was thought that the duplication would occur at a similar frequency. However, far fewer people were initially reported in the medical literature (about 50 were reported in 2011). Currently (2020) about 150 people have been reported in the medical literature. More people are still reported with the deletion, this is very likely to be due to the fact that the duplication is less severe and the features are highly variable (Velleman 2011; Morris 2015).

## What is the outlook?

Healthy people with 7q11.23 duplication syndrome are expected to enjoy a normal lifespan. Regular evaluation of aorta dilation is recommended.

## Pregnancy and birth

Mothers carrying babies with 7q11.23 generally experienced no pregnancy problems, had a normal delivery and only discovered their baby was affected after the birth (Unique). However, a few women have reported problems during pregnancy and some infants have required intensive care following birth (Morris 2015).

## Growth

Babies are often, but not always, of normal weight at birth. However, a few babies are small and underweight at birth, and a significant fraction are in the upper 5% of birth weights (Morris 2015). Birth weights recorded at Unique and in the published medical literature show a considerable variation with an average of 3.199 kilos (7lb 1oz) (Depienne 2007; Torniero 2007; Unique).

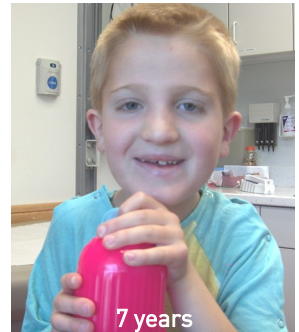
### Range of birthweights at Unique (at or near term):

2.721 kilos (5lbs 16oz) to 4.649 kilos (10lb 4oz)

Most babies and children identified so far have shown a normal growth rate after birth, although some have growth delay and remain short. Overall, no consistent effect on growth has been found (Somerville 2005; Berg 2007; Depienne 2007; Van der Aa 2009; Unique). More recent publications in the medical literature have identified a number of children with a 7q11.23 microduplication as having short stature, some of whom were also identified as having growth hormone deficiency (Morris 2015).

## Feeding

Most babies and children do not have feeding problems and many are able to successfully breastfeed, although one or two need tube feeding at first (Somerville 2005). Unique data show that many babies (6 out of 7) have gastro-oesophageal reflux (where feeds and stomach contents return into the food passage and are often vomited or may be inhaled, causing chest infections, known as aspiration pneumonia) but this has generally been well controlled by giving feeds slowly, positioning a baby semi-upright for feeds and where necessary raising the head end of the bed for sleeping. If these measures are not enough, prescribed medications or anti-reflux milk are usually enough to keep feeds down. Reflux has been described much less frequently in the medical literature. In only one case was reflux serious enough for hospital treatment (Berg 2007; Torniero 2007; Unique). A more recent research project (Morris 2015) described four young children as having significant problems with feeding requiring feeding via gastrostomy (one of whom was still tube fed at age 12 years).



Babies with a cleft palate can also find the action of sucking and swallowing difficult and two Unique babies with a cleft palate had feeding difficulties which resolved after surgical repair. One Unique child had no feeding problems as a baby but struggled initially when she started eating solid food and would choke very easily. However, the issue resolved and at 6 years old she ate normally. One child described in the medical literature had hyperphagia (increased appetite and consumption of food) (Depienne 2007; Unique).

In six Unique children (out of eight), and also in 66% of a series of children in the published medical literature (Morris 2015), constipation was a significant problem. Dietary changes and/or medication can help to manage constipation (Berg 2007; Van der Aa 2009; Unique).

## Appearance

Babies and children with this duplication look perfectly normal and would not stand out from a crowd of other children. Geneticists trained to note unusual features may find some but these do not add up to a typical, recognisable facial appearance. Specific facial features that may be more common in children with a 7q11.23 duplication include straight and neatly placed eyebrows, a high broad nose and possibly deep-set eyes, a short groove between the nose and the upper lip, a thin upper lip and a broad, prominent forehead. Three authors have commented on a slight asymmetry of the face and macrocephaly (a large head) has been reported in a few people (Somerville 2005; Berg 2007; Torniero 2007; Van der Aa 2009; Velleman 2011).



## Development: sitting, moving, walking (gross motor skills)

Some people with a 7q11.23 duplication will have entirely normal development, but often they are a little slow to reach their developmental motor milestones with delays in learning how to crawl and walk in comparison to other children, but have generally overcome their difficulties by school age. All people described in the literature and known to Unique were fully mobile although some older children still had minor problems with balance and gait (Somerville 2005; Berg 2007; Depienne 2007; Torniero 2008; Van der Aa 2009; Unique).

Individual babies start to sit between 6 months and 15 months (average 10 months). Independent walking was mastered between 12 months and 2 years 2 months (average 18 months). In some cases, there were difficulties with coordinating both sides of the body, and with balance, leading to difficulties standing on one leg, hopping, skipping and pedalling (Somerville 2005; Berg 2007; Depienne 2007; Unique).

One of the causes of the delay in mobility is low muscle tone (hypotonia), reported in as many as 70 % of children. This makes a child or baby feel floppy to handle but generally improves as children mature and may disappear with physiotherapy and exercises (Van der Aa 2009; Unique).

“He runs with an unusual gait and cannot ride a bike without stabilisers. He had a mobility pushchair and Pedro boots” – 7 years

“She continues to benefit from adaptive PE and is still a bit behind peers in motor activity. She is able to do most of the things she should, she is just not as strong/quick/independent/confident.



She has learned skipping this year with much assistance" – 8 years

"I would say that every milestone was delayed at least 6 months" – 10 years

"She learned how to ride a bike at 8 years" – 12 years

"Can be clumsy while walking or running and cannot ride a bike" – 14 years



## Development: hand-eye co-ordination and dexterity (fine motor skills) and self care

Some children are delayed in controlling their hand use while others develop within the usual time range. In Unique's experience, even slow-developing children have learned to feed, dress and care for themselves by school age and while they may take longer to learn how to cut, draw and write than other children, they still achieve these skills within a normal or slightly extended timeframe. One boy of 12 was described as 'impulsive' when carrying out fine motor tasks but was more controlled when prompted (Somerville 2005; Berg 2007; Depienne 2007; Unique).

In terms of self care, data from Unique and the medical literature suggests that children may be late to be toilet trained during the day (average age 4 years) and at night. In a child with a borderline or mild learning disability, it may not be appropriate for parents to expect toileting to occur at the same age as in other unaffected children (Depienne 2007; Unique).



"She is still in nappies" – 6 years

"He cannot cut with a knife and struggles holding pencils" – 7 years

"All her fine motor skills were delayed and difficult to overcome, from feeding to dressing herself. She had trouble drinking from a cup or using cutlery. She still struggles with using utensils or scissors" – 12 years

"She had difficulty in the past with cutlery, tying laces and holding a pencil – all fine now after occupational therapy input" – 14 years

## Speech and communication

Speech and language development tends to be delayed and almost all of those with a duplication of 7q11.23 seem to be affected. Children have early delays in learning to express themselves understandably in organised words and phrases. However, all older children and adults who have been fully described do speak and most of them eventually talk in phrases and sentences, many with no obvious difficulty. Despite this, it is clear that the range, severity and permanence of the effect on speech and language vary a lot between individuals. While some children have only spoken their first understandable words between the ages of 18 months and four years, their understanding has been

generally much more advanced than their ability to talk. Some children have been taught to sign or use picture exchange systems (PECs) and others have used a repertoire of gestures and become reasonably fluent communicators using these methods. Later stages of language development have also been delayed, with vocabulary increasing but not at the same rate you would expect in other children. Progression to two-word phrases and sentences has been noted after the age of six years. One report suggests that 15 % (4 children out of 26) have mild language delays; 35 % (9 children out of 26) have moderate delays and 50 % (13 children out of 26) have more severe delays.

Another recent study of 42 adults and children (aged 18 months to 61 years) found that receptive language skills (understanding of language) were less affected than expressive language (what they are able to communicate). Most of the toddlers in this study had very limited speech and few identifiable, meaningful words. Among 25 children (aged 4-17 years) more than three quarters had verbal apraxia and dysarthria (see box below) more than half had articulation problems. This study also looked at eight adults (28-61 years, all diagnosed with a 7q11.23 duplication after a child or grandchild was diagnosed). Most had learned to compensate for their difficulties; the errors they made were primarily in challenging multisyllabic words (eg aluminium) or tongue twisters (Somerville 2005; Kriek 2006; Berg 2007; Depienne 2007; Torniero 2007; Van der Aa 2009; Velleman 2011; Unique). More recently, 52 of 61 children (82%) were diagnosed with Speech Sound Disorder, with older children being less likely to have a diagnosis.

One child had speech delay but improved dramatically between the ages of 4½ years and 5 years, coincident with medication for severe anxiety (see [Behaviour](#) page 14) (Berg 2007).

**Verbal apraxia** – a person has trouble saying what he or she wants to say correctly and consistently. It includes speech planning symptoms such as speech that takes lots of effort; difficulty putting sounds and syllables together in the correct order to form words. Another common characteristic of apraxia of speech is the incorrect use of “prosody” — that is, the varying rhythms, stresses, and inflections of speech that are used to help express meaning.

**Oral apraxia** – includes non-speech planning symptoms such as groping while trying to protrude the tongue and difficulty producing sequences of oral postures (such as stick out your tongue and smile).

**Phonological disorder** or **articulation disorder** – children do not use some or all of the speech sounds expected for their age group.

**Dysarthria** – non-speech and speech problems such as weakness, low or high muscle tone, or poor co-ordination of the muscles themselves and voice differences.

**Speech Sound Disorder** – is a communication disorder in which children have persistent difficulty saying words or sounds correctly. Speech sound production describes the clear articulation of individual sounds (phonemes) that make up spoken words. Speech sound production requires both the knowledge of how speech sounds and the ability to coordinate the jaw, tongue, and lips with breathing and vocalizing in order to produce it. In most cases, children with speech sound disorder respond well to treatment and speech difficulties improve over time.

Pronunciation difficulties have been obvious, with children only articulating the first syllable of a word or not progressing beyond two-syllable words. When tested, hearing has been normal but specific difficulties making certain sounds of speech (such as l, r) have been described in both children and adults.

A small minority of babies are born with a cleft in part of the roof of the mouth; even after repair this can affect the quality of speech sounds and so compounds the difficulties that children face.

Speech therapy, sign language and picture exchange communication (PECs) have all been shown to be hugely beneficial (Velleman 2011; Unique).

“She can say three word phrases and also uses signing” – 6 years

“The sound of his voice is higher than a typical child. It is also more staccato” – 7 years

“He was late to start talking and now uses 2/3 word sentences. He also uses PECs and Makaton [sign language]. He has daily speech therapy at school” – 7 years

“She sometimes has difficulty figuring out the mouth movements for a new word or phrase and it helps to have her ‘watch my mouth’ to see it first. Generally though she is pretty easy to understand and does not have a lot of mispronunciations” – 8 years

“He didn’t speak until 3 years but doing well now. He has had lots of therapy and is still working on the ‘R’ sound” – 10 years

“She speaks in sentences but has trouble pronouncing clearly and inflections” – 12 years

“She has no problems speaking but sometimes jumbles her words. She had speech therapy when younger” – 14 years



## Learning

Most children and adults with a duplication of 7q11.23 have an intelligence that falls within the low average range, however a significant proportion experience difficulties that fall within the specific learning difficulties spectrum. These specific learning differences result in many children requiring special help in school. A recent study suggests that 61 % (39 children out of 63) have average or low average intelligence, 30 % (19 children out of 63) have borderline average intelligence or mild learning difficulties and only 8 % (5 children out of 63) have moderate or severe learning difficulties (Mervis 2015). Most children will attend mainstream school but some may need classroom assistance or special needs lessons; other children benefit from a special education school (Van der Aa 2009; Unique).

The expressive language delay does not appear to lead on to a comparable delay in reading. In Unique’s experience, children have been reading well by eight years. Families also report that memory is a strength. It is believed that visuo-spatial reasoning (recognizing visual patterns and drawing inferences from them) is relatively protected in most children with a 7q11.23 duplication, although this is not true of all children. One study found that children with 7q11.2 duplications performed well at non-verbal reasoning (Velleman 2011). Unique families report that their children draw relatively well and in an interesting way. However, writing skills and mathematics may be weak areas as may any learning area where children are expected to articulate their thoughts rapidly.

In a study looking at literacy skills in 12 school aged children (7-15years) they found that those taught to read by phonics (9/12) had reading skills in the average for the general population range. The children taught primarily with sight-word methods (3/12) had more difficulty with mild disability to low average range (Velleman 2011).

“ She has a very good memory and can write her name” – 6 years

“ He can draw pictures with specific details that a typical person wouldn't. He needs patient teachers and is able to learn better from someone who is patient enough to break it down piece by piece and make learning fun” - 7 years

“ He is about 18-24months behind at school. He has a very good memory and likes to know about the world and everyday life. He likes to draw and has just learnt to write. He is not good at learning in a classroom setting. He learns more when out. However, he loves school but lessons need to be engaging and quick” – 7 years

“ Her IQ has been measured between borderline and mild learning difficulties depending on who administers the test. She has quite a good memory and is good at anything 'hands on'. Her reading is good but she struggles with writing and maths. Anything abstract is difficult for her. It helps to show her how to do something rather than using lots of words to explain it. Allowing her processing time and time to figure some of it out on her own.

“ She needs patience!” – 8 years

“ She loves to draw and write stories, mostly stick people with lots of detail. She learns best by someone instructing her; she cannot just read and understand her lessons but can sometimes follow short, simple instructions” - 9 years

“ He is about a year behind academically but is great with phonics and has good computer skills. He reads chapter books and can write age appropriately” – 10 years

“ She is at an age appropriate level for her school work, although she struggles to understand maths concepts. She loves to write stories and draw. She is home-schooled and so is able to have 1:1 attention” – 12 years

“ She has a good visual memory and likes to read magazines sometimes. She is still learning how to read but has improved in the last year. She can write short sentences. She needs time and repetition and instructions broken down into small chunks” – 14 years

## Most likely features

### ■ Generally good health

Reports show that most people with a 7q11.23 duplication enjoy good health. As children they have the same frequent upper respiratory tract infections as other children but outgrow the tendency by six to nine years of age. Two children had their tonsils and adenoids removed, in one instance motivated by an attempt to solve sleep apnoea. One child had urinary reflux, corrected surgically (Berg 2007; Van der Aa 2009; Unique).

### ■ Palate

Four babies out of a total of 34 were born with a cleft lip or palate (roof of the mouth) or both and a further baby was born with an unusually high palate (Somerville 2005; Berg 2007; Unique). The lip and palate fuse from pieces that start on opposite sides of the head. Usually, the lip fuses around weeks 6-7 and the palate at around 12 weeks. A cleft occurs when the pieces come round but do not join. Defects in the palate are common in children with and without a chromosome disorder. The hard palate at the front of the mouth may be split or the split may be found further back in the soft, fleshy tissue at the back of the top of the mouth. Occasionally the split is only seen in the tissue that hangs down above the tongue at the very back of the mouth (uvula, known as a bifid uvula when it is split).

A cleft palate causes difficulties both in feeding and in speech production. Surgical repair of the palate eases these difficulties and may eliminate them altogether.

## ■ Seizures

Seizures have been reported in less than 25 per cent of people with a 7q11.23 duplication (Van der Aa 2009). First seizures emerged between seven months and 12 years and were generally well controlled with medication and some children were able to come off medication and remain seizure-free (Berg 2007; Torniero 2007; Torniero 2008; Van der Aa 2009; Unique). In one child 'paroxysmic episodes' were triggered by intense bouts of laughing after which the child went pale, stared into space and fell down without hurting himself (Depienne 2007).

Several children have had a brain scan (magnetic resonance imaging, MRI) with generally non-specific results showing a slight reduction in brain volume and white matter changes, but it is not clear what these changes mean. In only one child was there a structural abnormality of the brain, suggesting that this is not part of a 7q11.23 duplication syndrome (Berg 2007; Torniero 2007; Unique). Another possibility is that the structural abnormality described by Torniero (cortical dysplasia of the left temporal lobe) could be at the extreme end of the spectrum of brain abnormalities and that current MRI technology is unable to detect subtle abnormalities of brain wiring that could underlie the language deficits prevalent in 7q11.23 duplication syndrome.

A more recent publication describes findings from ECG (electroencephalography) and MRI (magnetic resonance imaging) results in 12 children with a 7q11.23 duplication (Castiglia 2018). Structural abnormalities of the central nervous system were detected, like ventriculomegaly, hypotrophic cerebellum, hypotrophic corpus callosum and hypoplastic temporal lobes. Only one of the 12 individuals suffered from seizures (during childhood), three others had abnormal ECG findings but had no visible seizures. Morris 2015 also showed that 81.6% of MRI studies showed structural abnormalities such as decreased cerebral white matter volume, cerebellar vermis hypoplasia, and ventriculomegaly (64 people were studied).

## ■ Constipation

A research study (Morris 2015) identified chronic constipation in 35 out of 53 children (66%), seven of these children had encopresis (involuntary defecation) and four children required hospital admissions for disimpaction (a treatment for fecal impaction) and colon clean out. Constipation should be actively managed at all ages to prevent such problems. The research study also identified one child who had a motility study demonstrating slow motility and required a colostomy. Another child was found to have low anal sphincter tone and two children were shown to have normal ganglion cells by bowel biopsies.

## ■ Joint laxity

A number of children and adults with a 7q11.23 duplication have lax, or loose, joints. Joint laxity has been described in six people in the medical literature, but has only been reported in one Unique child (Berg 2007; Van der Aa 2009; Unique).

## ■ Heart problems

Heart problems were reported to affect around 20 per cent of people with 7q11.23 duplication syndrome in 2013. The most common problem reported in four children was [patent ductus arteriosus \(PDA\)](#), failure of the ductus arteriosus (channel between the aorta and the pulmonary artery that takes blood to the lungs) to close). One child had two [ventricular septal defects \(VSDs\)](#) which are holes in the wall between the two pumping chambers of the heart (ventricles). This allows blood to flow from the left to the right

chamber, increasing the blood flow to the lungs. Treatment is determined individually. Small VSDs may close spontaneously; a larger VSD usually needs surgical repair to prevent lung problems that would develop from extra blood flow. One child had an [atrial septal defect \(ASD\)](#) which is a hole in the muscular wall between the two filling parts of the heart. Some blood flows through from the left to the right side, increasing the amount of blood flowing to the lungs. Treatment depends on the type of defect, whether it closes spontaneously and its size. Treatment can include medical management, taking medications to help the heart to work better, control of potential infection to the inner surfaces of the heart and surgical repair with stitches or a special patch (Kriek 2006; Van der Aa 2009; Unique).

Since this guide was first written (2007), and updated (2010 and 2013) further information regarding the structure of the aorta (the main artery of the body) in people with 7q11.23 duplication syndrome has been described (Zarate 2014, Parrott 2015, Guemann 2015, Lechich 2020). The most recent publication in the medical literature describes a retrospective study of 21 children with 7q11.23 duplication syndrome who were offered screening echocardiograms. The study identified a few important findings. All children with 7q11.23 duplication syndrome showed an increase in all measurements of the aorta compared to a group of control children (who did not have a 7q11.23 duplication and were shown to have a normal heart structure and function). A thinning of the sinotubular junction (STJ) was also found in all children with a 7q11.23 duplication. A further specific measurement, the 'STJ-to aortic annulus ratio' was significantly increased in children with the duplication. Apart from these findings concerning the aorta, no other significant cardiac findings or abnormalities were identified on echocardiograms. However, in an earlier publication (Morris 2015), neonatal diagnoses of cardiovascular problems included septal defects in two, subvalvar aortic stenosis in one, and PDA in four. Four additional children were diagnosed with PDA between ages 1 and 8 years. This research project identified 12 out of 26 people as having aortic dilation.

Aortic dilation can be treated with beta blocker therapy and/or surgery if needed. Regular monitoring of aortic diameter is therefore recommended.

## ■ Eyesight

Eleven children out of forty have some defect of vision or focusing. Difficulties, usually correctable by the use of glasses, include a squint (strabismus, inward or outward) seen in three children or/and astigmatism, when the cornea (the clear cover over the iris and pupil) is abnormally curved which has been reported in three children. The effect on vision is to make objects appear blurred. Sometimes the brain can compensate for astigmatism although it may be too strong for this to happen without the aid of glasses. Four people have long-sight (hypermetropia) and two children at Unique have Duane's syndrome (an eye movement disorder where the eye cannot move outwards) (Berg 2007; Torniero 2007; Van der Aa 2009; Unique). In a more recent study, six children were found to have esotropia (eyes that cross when trying to focus) and two children had exotropia (eyes that deviate outwards) (Morris 2015).



## ■ Hearing

Generally speaking children have normal hearing. Young children frequently have fluctuating temporary hearing loss caused by a build-up of fluid behind the eardrum (glue ear). Glue ear usually resolves as children get older and the ear tubes widen and become

more vertical resulting in improved drainage of the middle ear. Hearing loss caused by glue ear is usually temporary. However, persistent fluid in the middle ear and glue ear can reduce a child's hearing at a time that is critical for speech and language development. Therefore, while glue ear persists, many children will need a grommet (a small ventilation tube) inserted into the eardrum (Berg 2007; Unique).

Two children within Unique failed regular hearing tests despite normal hearing because they did not understand how to respond to noise. Parents may be well advised to draw this to the attention of whoever is doing the screening. One Unique child has been 40 per cent deaf from birth and is now on his second set of grommets (Unique). A publication in the medical literature identified three children with hearing loss; two of which wore hearing aids (Morris 2015). Thirteen of the children in this study also had chronic otitis media in early childhood and eight were treated with ventilating tubes.



## ■ Teeth

Generally speaking, children with chromosome disorders appear to have somewhat more dental problems than their peers. Dental problems seen at both Unique and in the medical literature include two children with misalignment of teeth (malocclusion), crowded teeth in one adult, and one child with relatively small teeth which were widely spaced. Regular and high quality dental care is recommended (Somerville 2005; Berg 2007; Van der Aa 2009; Unique).

## ■ Genitourinary anomalies

Minor anomalies of the genitals are common in babies with chromosome disorders, most often affecting boys. The most common problem is cryptorchidism (undescended testes). The testicles can be brought down by a straightforward surgical operation if they do not descend of their own accord in time. One boy has been described as having a shawl scrotum (the scrotum surrounds the penis, resembling a 'shawl') and another is described as having small genitalia (Berg 2007; Van der Aa 2009; Unique). In a more recent study, a renal ultrasound was performed in 22 individuals (Morris 2015), two boys were found to have hydronephrosis (build-up of urine in the kidney), one girl had unilateral renal agenesis (one kidney missing) and Mullerian agenesis (when the uterus fails to develop), and one girl had unilateral renal agenesis and uterus didelphys (a double uterus). The remaining 18 children had normal results.

## ■ Other

Other health concerns which may or may not be linked with the duplication include flat feet (Berg 2007; Unique); cubitus valgus – an increased angle at the elbow making the lower arms stick out more (Berg 2007); hip dysplasia, corrected by splinting or surgery (Torniero 2007; Unique); talipes (club feet) corrected with support shoes (Torniero 2007); café au lait spots or patches of dark/light skin (Berg 2007; Torniero 2007); torticollis (the head is tilted to one side) which resolved with physiotherapy in one child and improved after an eye operation in the other (Berg 2007; Unique). A more recent study identified three children as being tongue-tied and eight who had had their tonsils and adenoids removed. (Morris 2015).

## Behaviour

Researchers have drawn attention to the overlap between atypical behaviours in very young children with a 7q11.23 duplication and those with an autistic spectrum disorder (ASD) so that children may first be evaluated for autism though they may not formally meet the diagnostic criteria. Two Unique children have a diagnosis of pervasive development disorder – not otherwise specified (PDD-NOS), an ASD which tends to be milder than autism. However, the specific behaviours and their severity vary between individual children. One study suggests that people with a 7q11.23 duplication and ASD often have a highly sociable personality with people they know and are comfortable with (Berg 2007; Van der Aa 2009; Sanders 2011; Velleman 2011; Unique). A more recent report in the medical literature (Klein-Tasman and Mervis 2018) describes an elevated rate of ASD in children with 7q11.23 duplication syndrome in comparison to the general population. Sixty three children with a 7q11.23 duplication (aged 4-17) underwent a thorough assessment and 12 met the criteria for a clinical diagnosis of ASD (notably 10 were boys and two were girls). The research also mentions that symptoms of anxiety were common and could be mistakenly identified as symptoms of ASD.

Repetitive movements, repetitive behaviours, repetitive speech, using another person's hand as a 'tool', limited facial expressions, excessive orderliness (lining up toys), lack of emotional interest, sensory integration problems, difficulty switching routines and avoiding social gaze or contact have been identified in individual children.

A diagnosis of autism can be extremely helpful in accessing services and tailoring the educational and behavioural therapy to meet the specific needs of a child with autism. It is possible that some behaviours lessen and may vanish once speech emerges. This suggestion fits with the description of one 13-year-old girl as 'socially normal – naive, loving and quiet' (Torniero 2007). This is also backed up by a study of 30 children which found that although children had behaviour consistent with ASD (including shyness and repetitive behaviours); the children also had important characteristics that are not consistent with ASD. For example, in play sessions with their parents, the participants had social communication strengths including eye contact and clear pleasure in interacting with their parent, shared enjoyment and creative, imaginative play. The researchers suggest that the reluctance of children with 7q11.23 duplications to engage with people they do not know is likely to be secondary to their speech and anxiety problems (see below) rather than to ASD (Velleman 2011).

Social, stranger and separation anxiety can be quite acute and was scored high by Unique families; one 19-year-old girl suffered from panic attacks (Berg 2007; Unique). A recent study of 42 people with a 7q11.23 duplication found that around three quarters of the children had an anxiety disorder with around a quarter had separation anxiety. Another study involving 27 children (aged 4-13 years) found that just under a third (8 children out of 27) had separation anxiety (Velleman 2011; Mervis 2012). Three quarters of children and 60 percent of adults were reported to have at least one anxiety disorder diagnosis, most commonly social phobia or specific phobia (Mervis 2015). Selective mutism, a symptom of anxiety, was found in 30 percent of children.

Some children, possibly particularly boys, also scored high for aggressive behaviours such as hitting or pinching, although Unique children did not score high for self-harming behaviours such as arm biting. Some children have difficulties with mood control – they get overexcited rather than excited and can quickly lose their temper when frustrated – and many children, notably boys, reported in the medical literature (although fewer Unique families) show difficulties with attention, restlessness or activity levels. One adult has been

reported with Asperger's syndrome (an ASD that is characterised by significant difficulties in social interaction, along with restricted and repetitive patterns of behaviour and interests) (Kirchhoff 2007). Where Unique families do report difficulties with concentration, they temper their judgments with remarks such as 'when trying to teach him new things, he gets frustrated, or doesn't seem to be interested. Concentrates best when he is the one who initiates the idea, or has a desire to learn.'

Additionally, affected children are more likely than children without a 7q11.23 duplication to have attention deficit hyperactivity disorder (ADHD) which is characterised by restlessness and a short attention span. Around 35 per cent of children with a 7q11.23 duplication are reported to have a diagnosis of ADHD (Mervis 2015). In the medical literature there is a high rate of attention deficit and hyperactivity disorders in some of the children's close families, suggesting that in these families these behaviours may not necessarily be linked with the chromosome disorder (Berg 2007; Depienne 2007; Van der Aa 2009; Unique).

"She loves playing with her baby dolls and puzzles. She is a helpful little girl and will help with the housework including the washing up. She is a happy, loving and caring little girl and absolutely adores any kind of animal. She self-harms and has a padded helmet as she head-butts walls, the floor and doors and punches herself on occasion" – 6 years

"A sweet boy but can be irritable, temperamental and edgy" – 7 years

"He likes outdoor activities, pets and cars. He is a real character. He has ADHD; he is very hyperactive and restless" – 7 years

"She has a great sense of humour and loves to make people laugh. She is observant of people and can be quite aware of others' needs. She loves playing with her puppy, computer games and dolls. Her difficult behaviours include shyness, restlessness, and some hyperactivity alternating with very sluggish periods, whining and arguing. Management has included behavioural therapy and setting limits" – 8 years



"She can be unaware of others in public, will say or do things another child would be embarrassed to; shy on meeting new people but very friendly once she gets to know them and loves to hug them. Talks to herself when she gets upset or frustrated, which she does easily" – 9 years

"He had a diagnosis of PDD-NOS before the 7q11.23 duplication diagnosis. He is inattentive with some hyperactivity. He loves trees and playing outside. He is intolerant of others, doesn't like change, hates loud noises or distractions and can't handle it if he doesn't get his own way. He can be rigid and anxious and easily frustrated" – 10 years

"She loves the computer and playing with her Barbie dolls. She is very caring and always wants to do things for others or to send cards to anyone who is having a birthday. She is currently trying to raise money for a homeless shelter. She does not have a diagnosis of ASD although she does have some autistic tendencies" – 12 years

"She is very kind and will share anything she has. She is full of extremes – she can be happy-sad, cruel-sensitive, playful-frustrated. She also has difficulties with peer interaction. She can be overly loving for a teenager, but extremely shy and under confident in unfamiliar situations. She demands attention, but then cannot handle the attention and cannot accept praise" – 14 years

## Sleep

The majority of children go to bed easily at bedtime and sleep well. However, sleep problems affect some children. One Unique child continues to have night-wakings and wakes up very early in the morning. Three Unique children who are poor sleepers were prescribed melatonin; even with medication one takes a long time to fall asleep and has problems staying asleep. A further Unique child has frequent waking. Sleep problems have also been noted in the medical literature (Somerville 2005; Berg 2007; Unique).

## Puberty

There is very little information available on puberty in those with a duplication of 7q11.23 but it seems likely puberty generally proceeds as normal at the usual age (Kirchoff 2007; Unique). One girl was evaluated for late puberty (Morris 2015).



## Adults with a 7q11.23 duplication

Nineteen adults discovered they carried the duplication after the diagnosis of their child or grandchild. One had no medical concerns and works independently; another finished school and had no developmental delays; another had seizures as a child and had impaired language processing and expression skills and trouble with articulation (Kriek 2006; Berg 2007; Torniero 2008).

In one study, information on seven of the parents who transmitted the duplication to their children was collected. One father who passed the duplication on to two children had learning and behavioural difficulties (including anxiety and aggression) and language impairment. One mother had a history of language and motor delay but completed normal school and works as an office clerk. She has joint laxity. Another mother has mild learning difficulties together with autistic features such as poor eye contact. Another mother works as a care assistant but reported that she did not do as well at school as her siblings. Another mother did not speak until the age of 5 years and had congenital clubfeet and as an adult works as a saleswoman. Another mother had a history of learning difficulties and now works as a bus driver. A father has a history of learning difficulties and social impairment and was in special education. He was recently diagnosed with autism and self-harming behaviour (Van der Aa 2009).

Some of the parents had a history of motor and language delay or learning difficulties which eventually resolved and in adult life parents are usually employed and functioning well (Van der Aa 2009).

A 23-year-old man is also reported in the medical literature. He has learning difficulties and poor social skills but lives alone. He has been diagnosed with Asperger's syndrome (Kirchoff 2007). An 18-year-old Unique member is at college (Unique). Eight adults were diagnosed following the diagnosis of a child or grandchild. All had some difficulties with speech although not enough symptoms to have been diagnosed with speech delay. Most had learned to compensate well for their difficulties (Velleman 2011).

## Why are people with a 7q11.23 duplication so different from each other?

We don't understand this properly yet but a person's own unique genetic background and environment play a role.

## Why did this happen?

A blood test to check both parents' chromosomes is needed to find out why the 7q11.23 duplication occurred. In the majority of cases the 7q11.23 duplication occurred when both parents have normal chromosomes. The term that geneticists use for this is *de novo* (dn) which means 'new'. *De novo* 7q11.23 duplications occur when the parents' sperm or egg cells form or possibly during formation and copying of the early cells after the egg and sperm joined.



When sperm and egg cells form, chromosome pairs come together and swap segments, this is known as 'crossing over' and ensures that the genome of each egg or sperm is unique. To pair up precisely, each chromosome 'recognises' matching or near-matching DNA sequences on its partner chromosome. However, throughout the chromosomes there are many blocks of DNA that are so similar that mispairing can occur. In fact, these similar blocks of DNA, technically known as 'low copy repeats', are so common that they make up about 5 % of the entire human genome. At each end of the 7q11.23 duplication syndrome duplication there is one of these blocks and it is thought that they cause a mismatch that results in the duplication.

These genetic changes occur in everybody as a natural process, it's only when they affect an important gene (or genes) that they noticeably affect health and development.

Children from all parts of the world and from all types of background have 7q11.23 microduplications. No environmental, dietary or lifestyle factors are known to cause them. So there is nothing that either partner did before or during pregnancy that caused the duplication to occur and equally nothing could have been done to prevent it.

In around one quarter to one third of families, the duplication is passed from parent to child. Sometimes neither the parent nor the child appears to be affected. In other families, the parents are apparently unaffected but the children seem to be affected (Berg 2007; Kriek 2006; Morris 2015).

## Can it happen again?

Where both parents have unaffected chromosomes, it is unlikely that they will have another child with a 7q11.23 duplication. Where one parent has the same duplication as the child, the possibility of having another child with the duplication would usually be 50 per cent. In families where the parent appears to be unaffected but the child is affected, affects on further children cannot be predicted.

Parents should have the opportunity to meet a genetic counsellor to discuss their specific recurrence risks and prenatal diagnosis options.

## If one person in a family with a duplication of 7q11.23 is mildly affected, will others in the same family also be mildly affected?

Not necessarily. There is a lot of variation between different members of the same family. We know that if one person is mildly affected, others may be more severely and obviously affected.

## Could my child with 7q11.23 microduplication syndrome have similarly affected children?

Yes, this is perfectly possible in just the same way as a parent with the duplication can pass it on. We have not known about the condition for long enough to be certain if it affects fertility but since there are many examples of parental transmission it is likely that fertility will be normal. In each pregnancy, someone with the duplication theoretically 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 any learning difficulty they may have themselves (Van der Aa 2009; Velleman 2011).

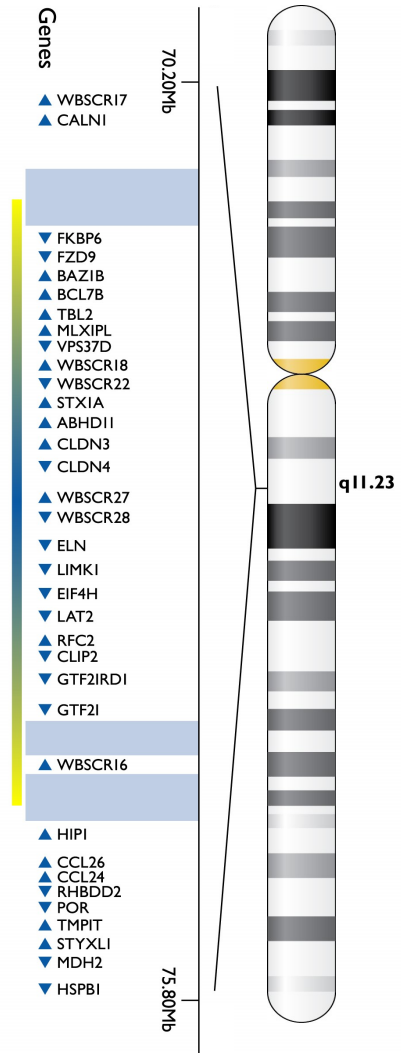
## Ongoing research involving 7q11.23

The features of a 7q11.23 duplication are likely to be a result of the extra copies of a number of different genes found in this region. The duplication is generally around 1.5 Mb and encompasses approximately 25 to 30 genes (Merla 2010).

Since speech delay is a common feature affecting those with a 7q11.23 duplication there are efforts by researchers to identify the gene(s) that may play a role in language development. However, since research into 7q11.23 duplications is in its infancy, it is not yet clear which of the 25 to 30 genes in this region are likely to play a role.

The genes *GTF2I* (general transcription factor 2-I) and *CLIP2* (cytoplasmic linker protein 2) have been postulated to be involved with learning difficulties, but further studies are needed to determine whether they have a role in the difficulties seen in people with a 7q11.23 duplication (Morris 2003; Vandeweyer 2012). The *GTF2I* gene has also been suggested to play a role in the separation anxiety disorder that affects some people with a 7q11.23 duplication (Mervis 2012).

It is important to remember that while identifying the gene(s) responsible for certain features of 7q11.23 duplication syndrome is interesting and may help guide future studies, it does not lead directly to immediate improved treatment. Additionally, even if the supposedly responsible gene is duplicated it does not always mean that the associated feature(s) will be present. Other genetic and environmental factors often have a role in determining the presence or absence of a particular feature.



## Chromosome 7q11.23.

The yellow-green-blue shaded bar (left) marks the Williams syndrome region. The genes in the region are listed. The thick blue horizontal bars mark blocks of DNA that probably cause both the deletion (as in Williams syndrome) and the microduplication to occur.

# Inform Network Support



Understanding Chromosome & Gene Disorders

**Rare Chromosome Disorder Support Group,**  
The Stables, Station Rd West, Oxted, Surrey. RH8 9EE, UK  
Tel: +44(0)1883 723356  
info@rarechromo.org | www.rarechromo.org

## Websites

<https://www.duplicationcares.org/>

Duplication Cares is committed to supporting families with children and adults diagnosed with 7q11.23 duplication syndrome, as well as being dedicated to raising awareness in the medical community about the existence and treatment of this disorder.

## Facebook groups

<https://www.facebook.com/groups/duplicationcares>

<https://www.facebook.com/groups/729341430825065>

<https://www.facebook.com/groups/2280027968680774>

<https://www.facebook.com/groups/7q11.23NL>

<https://www.facebook.com/groups/244955462195048>

## Join Unique for family links, information and support.

Unique is a charity without government funding, existing entirely on donations and grants. If you can please make a donation via our website at [www.rarechromo.org/donate](http://www.rarechromo.org/donate) Please help us to help you!

Unique mentions other organisations' message boards and websites to help families looking for information. This does not imply that we endorse their content or have any responsibility for it.

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. The information is believed to be the best available at the time of publication. It was compiled by *Unique* and reviewed by Dr Jonathan Berg, Department of Genetics, The University of North Carolina at Chapel Hill, USA, Dr Nathalie Van der Aa, Department of Medical Genetics, University Hospital University of Antwerp, Belgium and by Professor Maj Hultén BSc PhD MD FRCPath, Professor of Reproductive Genetics, University of Warwick, UK 2007, 2010, 2013. This guide was updated by Unique (AP) in 2020 and reviewed by Dr Lucy Osborne, Department of Medicine, University of Toronto, Canada.

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