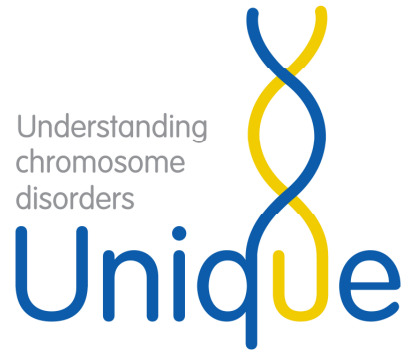


Understanding
chromosome
disorders



7q deletions between 7q21 and 7q32



rarechromo.org

Sources and references

Information is drawn from 35 cases: 15 in the published medical literature, 11 from *Unique*'s database; seven unpublished cases from the Chromosome 7 database housed at the Hospital for Sick Children in Toronto (www.chr7.org); and two cases from the Decipher database (<http://decipher.sanger.ac.uk>). Information varies from full developmental and medical data to a handful of salient features. So it's possible that some important information has been missed out, especially as regards development after babyhood and early childhood.

Some of the cases from the medical literature were published more than 30 years ago when equipment for examining chromosomes was relatively crude. In these cases the given breakpoints may not be as precise as they would be today (Ayraud 1976; Higginson 1976; Dennis 1977; Franceschini 1978; Hull 1979; Klep-de Pater 1979; Serup 1980; Abuelo 1982; Young 1984; Martin-Pont 1985; Fagan 1989; Morey 1990; Montgomery 2000; Scherer 2003; Feuk 2006; Cheong 2008; Marshall 2008; Decipher; Chromosome 7; *Unique*).

“Such a happy, loving child, he brightens up our day.

“He is always willing to assist. His delight in the simple joyful things is infectious and very levelling. From a difficult baby, he has grown into a kind, thoughtful adult who is looking forward to some independence at residential college.

Deletions on chromosome 7 between 7q21 and 7q32

People with a 7q deletion have some DNA missing from one of their chromosome 7s. The missing piece raises the risk of development and learning problems and physical abnormalities. But there is wide individual variation of what the impact may be.

Genes and chromosomes

Our bodies are made up of billions of cells, each containing about 30,000 genes. Genes act like a set of instructions, directing our growth and development and how our bodies work. Genes are carried on structures called chromosomes. There are usually 46 chromosomes, 23 inherited from our mother and 23 inherited from our father, so we have two sets of 23 chromosomes in 'pairs'. Apart from two sex chromosomes (two Xs for a girl and an X and a Y for a boy) the chromosomes are numbered 1 to 22, generally from largest to smallest. Each chromosome has a short arm (at the top in the diagram on page 3) called p from *petit*, the French word for small, and a long arm called q (at the bottom).

For healthy development, chromosomes should contain just the right amount of material – not too much and not too little. People with a 7q deletion have one intact chromosome 7, but the other is missing a piece, which can affect learning and physical development. Most of the clinical difficulties are probably caused by the presence of only one copy (instead of the usual two) of a number of genes. As a medium-sized chromosome, the 1150 genes on chromosome 7 represent about 4 per cent of the total number of genes in the human genome, the genome being the complete complement of chromosomes in each cell. However, a child's other genes, environment (including things like diet, exercise, exposures, upbringing) and personal characteristics also help to determine their future development, needs and achievements. Ultimately, the clinical outcomes will most likely depend on which of the genes in the 7q21-32 region are missing and which ones remain as duplicates.

How did the chromosome alteration happen?

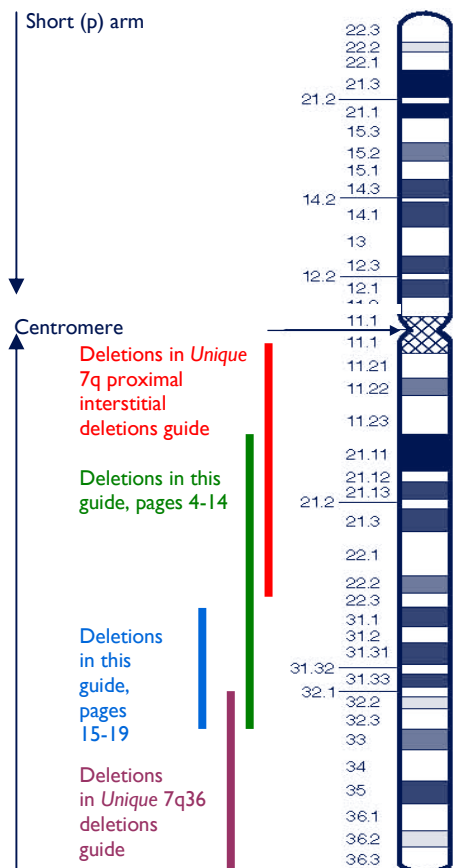
When a sperm cell from the father and egg cell from the mother first join, each typically carries just one copy of each chromosome. Together they form a single cell that now carries two copies of each chromosome. This cell must make many copies of itself (and all the chromosomes and genetic material) in order to make the trillions of cells that form into a human during development. Sometimes during the formation of the egg or sperm cells or during this complicated copying and replication process, parts of the chromosomes can break off or become arranged differently than usual. People with a 7q deletion have one intact chromosome 7, but a piece from the long arm of the other chromosome 7 is missing. Although the exact numbers and types of genes that are affected by the deletion are often not known, since some genes are missing there can be effects on development. So it is believed that most of the clinical difficulties are probably caused by having only one copy (instead of the usual two) of a number of genes. We are still learning about the specific jobs or functions of the genes that are sensitive to copy number (ie. 0, 1 or 2 copies). Also, it is important to reiterate that a child's other genes, environment and unique personality also help to determine their future development, needs and achievements.

Looking at chromosome 7q

Chromosomes can't be seen with the naked eye, but when stained and magnified under a microscope, each one has a distinctive pattern of light and dark bands. Looking at chromosomes in this way, it is possible to see where the chromosome has broken and what material is missing, if the missing piece is large enough. A missing piece visible under the microscope is called a **deletion**.

In the diagram on this page you can see the chromosome bands are numbered outwards from the point where the long arm meets the short arm. In a 7q21q31 or q32 deletion, the chromosome has broken in two separate bands, leaving out the chromosome material between them. This is called an **interstitial deletion**.

Sometimes a deletion is so small that it can only be identified using molecular or DNA technology, in particular a technique using microarrays (array CGH). This technique shows in great detail gains and losses of tiny amounts of DNA throughout the chromosomes and can also show whether particular genes are present or not. A deletion so small that it can only be identified in this way is called a **microdeletion**.



Results of the chromosome or array test

After their chromosomes are tested, your child will almost certainly be given a karyotype, a shorthand notation for their chromosome make-up. It is likely to read something like this:

46,XY,del(7)(q22.1q31.2)dn

46 The total number of chromosomes in your child's cells

XY The two sex chromosomes, XY for males; XX for females

del A deletion, or material is missing

(7) The deletion consists of material from one of the two chromosome 7s. The other is intact

(q22.1q31.2) The chromosome has broken in two places. The first break is at q22.1 and the second break is at q31.2 and the material between is missing

dn Short for 'de novo', meaning 'new event'. The parents' chromosomes have been checked and no deletion or other abnormality found. The deletion has not been inherited.

If your child has a chromosomal microarray test, which scans the chromosomes for imbalances at a higher resolution than karyotyping, the results are likely to read something like this:

arr cgh 7q21.11q32.3(85,133,634-132,234,884)x1

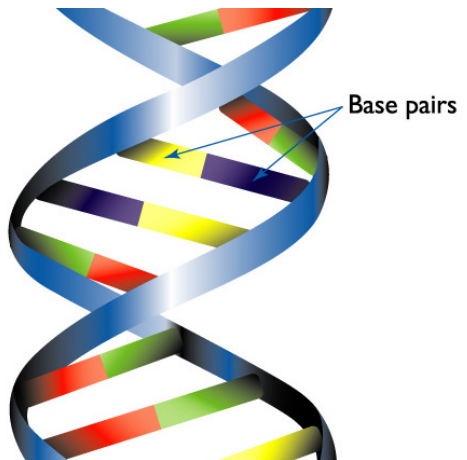
arr cgh

The analysis was by array CGH

7q21.11q32.3

A change was found starting in band 7q21.11 and ending in band 7q32.3

(85,133,634-132,234,884)x1 The first base pair (the chemicals in the DNA molecule that form the ends of the 'rungs' of its ladder-like structure, see diagram) shown to be missing is number 85,133,634 counting from the top of the chromosome. The last base pair shown to be missing is 132,234,884. Take the first number from the second number to give the number of base pairs missing, ie 47,101,250. This can also be expressed as the rounded number of 47 megabases (or 47Mb).



Are there people with a 7q21q32 deletion who are healthy, have no major medical problems or birth defects and have developed normally?

So far everyone we know about who carries a 7q21q32 deletion has experienced at least some developmental delay and has needed support at school with their learning. In the *Unique* group the degree of delay ranges from mild to severe. While most babies are born with a healthy heart, defects have been found in more than one third. And while most children do not develop epilepsy, almost one in three babies or children has had seizures.

Learning

The chromosome deletion is likely to affect a child's ability to process, retain and use information, but there is a range from mild or more likely moderate to severe effects. Even children who are severely affected are capable of subtle and complex learning, may well have areas of particular ability such as long term memory, music or spatial memory and may acquire some literacy and computer skills. Children who have lost the *FOXP2* gene at 7q31.1 are likely to face particular difficulties with speech and language (Klep-de Pater 1979; Abuelo 1982; Chromosome 7; Decipher; *Unique*).

“ She attends a special school where there is a 1:2 staff ratio plus full therapy support. She likes riding, yoga, swimming, water and messy play but he finds concentration especially difficult. She is sociable, which supports her learning. 1:1 support and picture exchanges are the most helpful learning approaches. She doesn't read but will listen to stories for a short time - 6 years

“ He attends a regular school with a special education room. Currently he is having major difficulties with school as they are unable to figure out how to teach him. His difficulties are general but especially with maths. His learning is helped by being happy, social, a big helper and wanting to make others happy. He reads short, simple words – I, me, the, he, she – and types with 1 or 2 fingers on a keyboard - 8 years

“ When he was 6, he could read 2 or 3 words and write his name backwards. Now he is operating at around half his actual age. He loves using the computer, prefers numbers to literature and language and finds reading and writing especially difficult. He learns best with constant praise and 1:1 teaching. He can match about 15 words with pictures and read about the same with much prompting. He can write his name and draw a face or person; all other drawings are difficult to identify. He can use a computer keyboard slowly and is better with a mouse. He loves anything with wheels, programs such as Chuggington [trains], playing the Wii, especially racing games, playing with others, kicking a ball, playing on the trampoline and riding his trike - 11 years

“ At 5, she could recognise her own name and while she could not write yet, she could operate the keys or mouse on a computer. Her memory was considered very good. She loved music and dancing and had a lively, positive and determined personality, as well as being inquisitive. Her school noted that she could match by colour and match objects to pictures. At 11 years, she can read very simple words, possibly at the level of a 5/6 year old. She loves music and dancing and enjoys numeracy but finds literacy and reading especially difficult. She attends a special needs school in a small class with lots of speech therapy and does best with one to one teaching - 11 years

“ She was reading and writing by 6½. She learns more slowly than others and does best with as much 1:1 as possible. She now attends a private special needs school where she is especially good at science and computers but finds mathematics and reading difficult. She is very determined: if she likes something, she will learn about it. She is currently reading 3rd grade easy readers, can write sentences and has very good keyboard skills. She enjoys TV, videos, computers, music, laptop, the internet and ITouch - 15 years

“ He attended a school for people with severe learning difficulties, had a statement of special educational need and started to read and write at the age of 10. Despite a short attention span, he made steady progress at school and was reading 'easy' books at the age of 13, accessing text supported by symbols. He enjoyed finding information from

pictures and looking at factual books. He remained clumsy but his writing became easier to read. He could write several words independently especially on a computer but found sequencing a sentence hard. He had good keyboard skills, could process and use a variety of keys, access the internet independently and search for his interests. His learning disability was rated severe. He has a good memory for events and facts and good general knowledge as well as many practical and problem-solving skills. He uses initiative well and has good observational skills and a good sense of humour - 17 years

Speech and language

Speech and language delay is likely to be an area of special concern. Where the deletion includes the part of the 7q31.1 band that contains a 'speech and language' gene called *FOXP2*, a disorder known as developmental verbal dyspraxia may emerge. Someone with developmental verbal dyspraxia has difficulty making and coordinating the movements needed for spoken language. The severity seems to depend on whether the *FOXP2* gene [between base pairs 113,841,565 and 114,121,063] has been lost from the chromosome 7 inherited from the father or from the mother. Where the deleted chromosome 7 has come from the father, so there is no paternally-inherited *FOXP2* gene, the developmental verbal dyspraxia will be much more severe.

All areas of speech and language are involved but expression [speaking] is much more affected than receptive language [understanding] and articulation [making speech sounds] is most severely affected. It is very likely that a developmental assessment will show that speech and language are more delayed than other areas of development and language will appear disordered. Some babies do not cry initially, making at most very feeble sounds for the first days. The weak, plaintive and cat-like cry of some babies can last for months but generally matures into a normal-pitched voice. There may be further early signs with babies having difficulty swallowing, and choking and inhaling feeds may have occurred; later on, chewing is difficult. Difficulties coughing, clearing the throat, sneezing and laughing ['like a squeal'] are common and most children cannot blow their noses. Some have difficulty lifting their tongue and moving it from side to side as well as pushing their lips forward; dribbling [drooling] may be very evident.

Some babies never babble and typically children say their first words quite late [from around 3]; those who progress to combining words do not do so before the age of 4. They have a limited vocabulary and their speech is limited to simple sounds. A speech and language report on one 4-year-old child records a limited repertoire of consonants, many sounds omitted and replaced with a glottal stop and many vowel sounds distorted. Speech can often not be understood outside the family, which has an obvious impact on children's ability to socialise. The evidence from *Unique* suggests that difficulties persist with some improvement.

Among *Unique* members, speech delay is universal but children generally want to communicate so they use other means drawn from a 'total communication' repertoire: gestures, noises, pushing/pulling, facial expressions, signing and communication aids (Abuelo 1982; Feuk 2006; Chromosome 7; Decipher; *Unique*).

" No speech although more sounds are coming. She uses gestures, vocal noises, pushing/ pulling and facial expressions. Her understanding is good and she understands basic signing but doesn't sign back, watching your face for guidance - 6 years

“ He no longer needs a Dynavox communication device for speech. He is now verbal but difficult to understand by strangers. His receptive language is much better. He used single words at 2-3, mostly 3-4 word sentences at 4-5 and now longer sentences that can be 8+ words long. He often confuses words like *I* and *me*, eg ‘*me go to the park ...*’ and



8 years

has difficulty with many sounds of speech as he has low oral muscle tone - 8 years

“ At first she used Makaton signs but by 2 she was starting to say a few words and a year later she could say *no*, *bye bye*, *all gone*, *more* and *ball* as well as joining 2 or 3 words together. Her understanding was very good but she had real difficulties in pronunciation and expression. She had a limited range of consonants, left certain sounds out or replaced them with a glottal stop and distorted vowels, making her speech difficult to understand. Only her mother could understand some words. At 4 her speech and language difficulties were described as ‘considerable’. At 11, she still has difficulty with all sounds and her speech remains difficult to understand and very disjointed. However, she picks up new signs quickly and uses them and will persist to get her message across. She sometimes prefers to use pictures and her communication book to communicate. When unsettled, she tends to stammer. Her understanding is relatively strong and simplified language helps. She tries to interact with other children but her difficulties make this hard so she often prefers to play on her own - 11 years

“ His early ‘baby’ sounds were very limited with first words at 4. He now communicates vocally, signing, pushing and pulling. He has very good understanding but poor expression and speech. He needs signing to reinforce the message and finds this difficult due to motor skill problems. He can say 3-4 words but is unclear to people outside the family. Today he usually uses no more than 3 words and has great difficulty putting speech sounds together. He can say some single letters very clearly on their own but cannot put them together eg *boat* is *dote*; *plane* is *dane*; *max* is *ats* - 11 years

“ Her first words emerged by 3½. She now communicates using speech in 5-6 word sentences but leaves off the ends of words and sometimes gets lazy and slurs sounds. Her receptive language is much better than expressive - 15 years

“ His cry as a new baby was high-pitched and distinctive. His speech remained limited to occasional words and syllables and he might put two words together or just use one syllable of a word. Using a Casio Chat PC, his communication skills were excellent and he understood very much more than he could express. He has severe dyspraxia and articulation problems but no difficulties communicating and is very sociable and inventive. Speech therapy began at the age of 2 and was ongoing - 17 years

Sitting, walking, running

Some delay is typical but from *Unique*'s experience, it may be insignificant or much more obvious. Babies rolled over between four and 18 months, sat between six months and three years, became mobile between 10 months and 2½ years and started walking between 16 months and seven years. Muscle tone is typically altered. Typical patterns are either low muscle tone in the upper body (so it feels floppy) and high tone in the lower body (so the legs feel taut and a child tends to walk on their toes); or generally low tone. Some children wear supportive gaiters, splints or orthotics; they may need a stander and a walker when learning to walk. Physiotherapy is extremely helpful and some children with high tone in the lower body are further helped by surgery to lengthen tendons in their legs (Abuelo 1982; *Unique*).

“ She started walking at 5 years, 3 months. Today she walks but needs a pram for longer periods outside and needs assistance on stairs. She enjoys riding, swimming and pushing a doll's pram - 6 years

“ She walked at 22 months but was quite clumsy and fell and bumped into things frequently. She could ride a bike with stabilisers at 5, liked dancing but could not yet swim. Now she enjoys swimming and going out on her bike or scooter - 11 years



Similar deletion: different children
Left: 5 years Right: 14 years

“ He walks in a plodding manner and often falls. Although he can move around unaided, he is clumsy. He sits by slouching against a chair and prefers support. He enjoys playing football and riding his trike - 11 years

“ Her mobility is normal but she runs more slowly than most children. She enjoys swimming, riding, baseball and soccer - 15 years

“ Mobility development was scarcely delayed as he crawled at 10 months and walked at 16 months. By 13, he was cycling, skateboarding and could swim a length, play football and dance in a slightly uncoordinated way - 17 years

Using their hands – fine motor control

“ Independent in personal care - 8 years

“ She still needs help to brush her teeth, bathing, washing her hair and dressing and still finds it difficult to do buttons, zips and fasteners. She is still quite clumsy and will drop and spill things - 11 years

“ Can toilet, shower, bathe, hairwash, dress etc independently - 17 years

Social behaviour

Evidence from *Unique* suggests that children are generally happy, sociable and want to interact with others, particularly people they are familiar with. Some children may show anxiety in unfamiliar surroundings. Behaviours like intermittent aggression [pinching, hair pulling] and defiance [stamping, shouting, stubbornness, pulling away] respond as in any other child to firm, consistent training and positive reinforcement as well as modelling techniques like social stories. Two children have a diagnosis of autistic

spectrum disorder and need firm, clear, planned routines. It is not yet clear if the *FOXP2* deletion is sufficient to cause autism or if perhaps changes in other genes are also involved. Two other children were treated with medication [Adderall, Strattera, risperidone [Risperdal], methylphenidate [Metadate], guanfacine [Tenex]] for attention deficit hyperactivity disorder [ADHD] but one outgrew this behaviour as a teenager. Around half of *Unique* families needed some professional help [developmental nurse; educational psychologist] with their child's behaviour.

Children who are missing the *FOXP2* gene on 7q31.1 and are thus at risk for developmental verbal dyspraxia face particular problems with socialisation as their language is frequently incomprehensible to people outside their close family (Decipher; *Unique*).

“ She is generally content, likes time interacting and time on her own but enjoys adult attention. She has tense moments during the day when she shows her challenging behaviours - 6 years

“ Very happy and unaware of his special needs, he brings a lot of happiness to all of us. He interacts well with those he knows but not with those he doesn't, hiding and avoiding eye contact. A really happy soul - 11 years

“ She still gets upset very easily and can cry over small incidents or when she is corrected. She is a cooperative, enthusiastic friend who has her own ideas but can also follow others, making her popular amongst her peers - 11 years

“ Transitioning can be difficult but she is warned in advance. She is almost too sociable: she likes to tell stories, even to strangers. A very happy kid – she reminds us to smile daily! No problematic behavior now - 15 years

“ Very boisterous but generally pleasant, helpful and sociable and game for anything! He enjoys helping out and being involved with others. He is inappropriately friendly and would go off with a stranger. When cross he now raises his voice and is very much ‘in your face’ which can be difficult, given his adult height. We have always encouraged him to do what ‘normal’ children do and he will have a go at everything - 17 years

Sleep

Sleep difficulties are common among both typically developing children and those with chromosome disorders. Strategies are generally the same whether a child has additional special needs or not. Among children with a 7q21q32 deletion, 2/4 children have a problem with sleep. One child, a boy of 11, wakes frequently at night and sleeps in a lit room as he is frightened of the dark. A fixed bedtime routine helps but he needs constant reassurance that someone is close by as he goes to sleep. A teenage girl of 15 has difficulties getting to sleep, which her parents handle by giving her warm milk and allowing her to watch a movie as she falls asleep.

Pregnancy, birth and newborn

Among the eight pregnancies we know about, there was excessive amniotic fluid [polyhydramnios] in three. In one of these pregnancies, the amniotic fluid reduced after the due date and birth was eventually induced at 10 days after term. Three/18 babies were born early at 34-35 weeks, but the rest were born at or near term. Birth weights at term ranged from a low 3 pounds 5 ounces [1.5 kg] to a normal 7lb 14oz [3.57kg].

Average birth weight among 18 babies was 5lb 15oz [2.687 kg], which is low. One baby was small for gestational age despite the mother having pregnancy-induced diabetes, which is usually associated with large babies. Despite these low birth weights, only one baby's small size was picked up during pregnancy.

As far as is known, delivery was usually uneventful but two babies were born by emergency Caesarean section. One of these babies had low muscle tone and the Caesarean followed a traumatic failed vaginal delivery. We don't know much about babies' condition but Apgar scores - a measure of well-being at birth - were generally reasonable [6-10/10]. Individually, some babies had problems in the newborn period: episodes of turning blue; unusual breathing, choking and gagging; and seizures. A plaintive, single-tone, cat-like cry has been remarked upon repeatedly but not noted among *Unique* families, although a faint cry or no cry has (Hull 1979; Serup 1980; Abuelo 1982; Fagan 1989; Montgomery 2000; *Unique*).

“ Very sick and colicky as a newborn - 17 years

Feeding

Early feeding difficulties are extremely common but not universal among babies with a 7q21q32 deletion. They are due in part to babies' low muscle tone and lack of control of the muscles in the mouth and throat. The most common complaints are of weak sucking, unco-ordinated swallowing and the lack of a cough, leading to choking while eating. Gastro-oesophageal reflux – where the stomach contents return up the food passage and may be inhaled – is also common and can be severe. These challenges are most likely related to having only a single *FOXP2* gene. Careful positioning for feeding, feed thickeners and prescribed medicines to inhibit gastric acid may control reflux but some babies benefit from a fundoplication, a surgical operation to improve the valve action between the stomach and food passage while others need to be fed through a gastrostomy, a tube direct into the stomach (Franceschini 1978; Abuelo 1982; Martin-Pont 1985; Fagan 1989; Morey 1990; Montgomery 2000; *Unique*).

“ She did not manage to breast feed and struggled with a bottle. Reflux was confirmed by a pH study and she aspirated her feeds. Milk feeds were thickened and food puréed until she was 18 months as she choked on lumps. Video fluoroscopy confirmed her swallowing problems and she could not cough effectively, but by 2 she was eating finger foods and by three feeding was normal and she had a good appetite and ate a varied diet. She still struggled with chewing some foods and occasionally choked - 5 years

“ She had a tendency to choke on lumpy foods so everything was liquidised until she was 4. She needs a sauce to help food down and it is still cut up very small. She can manage some finger foods, such as breadsticks, cooked carrot and toast but finds it difficult to drink water and prefers milk as it is slightly thicker - 6 years

“ At birth he found latching on hard, tired easily and was often sick. Today he is limited to foods he can control orally like bread and toast. His food is cut up; his chewing is poor and he uses his tongue to squash food on his palate. He uses a beaker - 11 years

“ She tried to breastfeed but had a very poor suck and also had reflux for the first 9 months. Today she has no problems with eating and drinking although she doesn't use a knife yet - 15 years

“ Breastfed but very sick, always brought back part of feed - 17 years

Growth

Growth after birth is typically slow or normal, with individual babies whose energy intake is boosted catching up lost height. Some small for dates babies grow at a normal rate throughout childhood. Most children are short or of average height, usually proportionate but one child is described as 'solid', while another is lean. Very short stature, below the lowest curve on the growth chart, is unusual (Hull 1979; Klep-de Pater 1979; Fagan 1989; Chromosome 7; *Unique*).

“Average height: short legs, longer body, average build but tummy protrudes - 6 years

“Tall, lean, very little fat - 8 years

“Small for age and very slim - 11 years

You may notice

■ Facial and teeth

You may notice that your child looks different to other family members.

The differences may be slight or more striking. Looking at the pictures in this guide, you may see similarities with your child. One *Unique* family remarked that their daughter had the look of a child with Down's syndrome, but this isn't obvious in other children. Typical features remarked upon by researchers and *Unique* families include: a pixie-like face, due partly to having a small chin and lower jaw; a large mouth with downturned corners; low ears, sometimes with an unusual shape; small eyes that may slant upwards; a flat bridge to the nose.

Two *Unique* families remarked that their child's teeth stuck out at the front; after bracing they 'look beautiful'. Another child had late-emerging adult teeth: at 11, he had six adult teeth. Another 11-year-old has impacted teeth with no adult teeth to come through in some places, leading to gaps in her front teeth (Martin-Pont 1985; *Unique*).

■ Hands

Where material is missing from band 7q21.3-q22 at a site known as *SHFM1* (split hand foot malformation 1), one or both hands or feet may be split, with missing fingers or toes and webbing between the remaining digits. When one hand or foot is affected, it is more often the right one. But even when *SHFM1* is missing, not everyone has the hand-foot anomaly (Higginson 1976; Klep-de Pater 1979; Morey 1990; Cheong 2008).

Your baby's hands may have other, much less obvious but still slightly unusual features. Many of these features are not specific to babies or children with a 7q deletion but are also found in other chromosome disorders. They include a single or otherwise unusual palm crease; extra fingers; tightly contracted fingers; a thumb formed like a finger; short finger bones; tapering fingers; index fingers curled in towards the palm at birth; stubby thumbs; inward-curving fifth fingers [clinodactyly]; short, plump fingers; small hands; long, spidery fingers; very stiff hands with many double-jointed joints (Franceschini 1978; Hull 1979; Serup 1980; Young 1984; Morey 1990; Scherer 2003; Cheong 2008; Chromosome 7; Decipher; *Unique*).



Persisting tendency to use the middle rather than index fingers

■ Feet

Apart from the split foot anomaly, which typically affects both feet, a number of other unusual features of the feet have been found in individual babies and children. These are obvious at birth and don't develop later. The problem may just be cosmetic, it may be correctable with physiotherapy or it may need splinting and sometimes surgery. The feet may be at an unusual angle to the legs, or may not flex upwards [foot drop]. One or more toes may be oddly positioned, they may be bent or overlap, or they may be joined by a bridge of skin and tissue. The toe nails may be unusually formed (Higginson 1976; Martin-Pont 1985; Montgomery 2000; Chromosome 7; *Unique*).

■ Minor genital anomalies

Minor genital anomalies appear to occur at an increased rate in babies with chromosome disorders and were found in 8/35 children with a 7q21q32 deletion. In boys, these include undescended testicles, an unusually small penis, hypospadias, where the hole normally at the end of the penis is on the underside instead and more unusually in a girl an enlarged clitoris. A hydrocele, causing fluid to gather round the testis in the scrotum, and hernias in the groin have also occurred. Some minor genital anomalies can be left while others are corrected by surgery (Dennis 1977; Serup 1980; Young 1984; Martin-Pont 1985; Morey 1990; Montgomery 2000; *Unique*).

Clinical concerns

■ Heart

A range of simple and more complex heart problems has been found in 13/35 affected babies. Some have needed surgical repair; in other cases we do not know if the problem needed treatment or resolved naturally over time. The most common problem is a hole either between the upper collecting chambers of the heart [atrial septal defect/ASD], between the two lower pumping chambers [ventricular septal defect/ VSD], or both. A narrowing or thickening of one of the valves leading to a blood vessel [aortic stenosis; pulmonary stenosis] has also been seen repeatedly, in two babies together with a VSD. Two babies were born with very complex heart problems and sadly one of them did not survive (Higginson 1976; Dennis 1977; Franceschini 1978; Martin-Pont 1985; Fagan 1989; Morey 1990; Montgomery 2000; Chromosome 7; *Unique*).

■ Seizures

Eleven/ 35 babies or children have had seizures although not all have been diagnosed with epilepsy. Two young children had febrile convulsions and one was treated with anti-epileptic drugs until she was 6. In most cases, the type of seizure was not specified but one baby had neonatal myoclonus [twitching of arms and legs when asleep] until the age of four months with no recurrence by the age of 11 and another child who had myoclonic seizures came off medication at the age of 5. [A myoclonic seizure is a sudden jerk-like movement that may involve the limbs on one side of the body or both, the neck or trunk.]

In all, four children outgrew their seizures, including a baby who had a single seizure at 4 months and a boy of 13. Medication usually controlled the seizures but they continued despite medication in one 22-month-old baby.

Infantile spasms [a type of seizure usually occurring in clusters in babies between 3-10 months, seen most often when a baby wakes] are suggested to be caused by the loss of a gene in 7q21, the *MAGI2* gene. Deletion of the *SGCE* gene on 7q21.3 from the chromosome 7 inherited from the father (less often from the mother) is believed to underlie myoclonic seizures [generalised seizures involving jerky or shock-like contraction of different muscles anywhere in the body but usually the arms or legs] (Higginson 1976; Franceschini 1978; Abuelo 1982; Young 1984; Fagan 1989; Marshall 2008; Chromosome 7; *Unique*).

■ Respiratory infections and general wellbeing

Young children are vulnerable to infections of the respiratory tract and some children with chromosome disorders, including those with a 7q21q32 deletion, are especially vulnerable. This is due to a combination of factors: in some, a tendency to inhale part of feeds, setting the scene for an infection in the lungs, and underlying low tone, making coughing up secretions difficult, play a role. The absence of a cough reflex in some young children with a 7q21q32 deletion makes them especially vulnerable. One child had tracheomalacia, where the cartilage rings that keep the windpipe open are too soft, so the airway can close off more than it should. This usually causes noisy breathing that is worse when the child is crying, feeding or has a cold and doesn't respond to standard asthma treatments. If the child has an infection they may need hospital treatment or ventilation. Tracheomalacia gradually improves with age and is usually not a problem after the age of 2.

As children grow and mature, their resistance improves but *Unique's* experience is that many children have very frequent chest infections especially in winter and these may be severe enough to need hospital treatment. Some young children are given protective antibiotics throughout the winter (Higginson 1976; Klep-de Pater 1979; Young 1984; Fagan 1989; Feuk 2006; Chromosome 7; *Unique*).

“ At 6 months she had never coughed and had caught bronchiolitis and further chest infections which remained frequent, requiring on occasion intravenous antibiotics and regular antibiotic treatment. When she has a cold or infection, this affects her sleep and she is often sick in the night - 5 years

“ She was tested for cystic fibrosis but was clear. Her tendency to chest infections lasted until she was 3 - 6 years

“ He often gets colds and temperatures. He suffers more in winter, gets sore throats and mouth ulcers and bacterial skin infections frequently. He is happy in himself but has many minor illnesses - 11 years

■ Head and brain

Your baby's head may look an unusual shape or size. Most commonly, children have somewhat small heads [microcephaly 8/35], but some have a large head. Less commonly your baby's head may be an odd shape, flatter on one side than the other or shaped like a parallelogram when viewed from on top [plagiocephaly]. One cause of plagiocephaly is early fusion of one of the seams between the bony plates of the skull. In one baby these seams were wide open at birth and the soft spot on top of the head [fontanelle] was very large.

Most children do not need any imaging of their brain, but where this has been

undertaken, it has shown a shrinking of the brain [cerebral atrophy] in three children and excess fluid or unusually large fluid-filled spaces [ventricles] in two children. In two children the band of 300 million or so nerve fibres that link the brain's two hemispheres was underdeveloped or missing [agenesis of the corpus callosum/ACC]. The effects of ACC range from subtle to severe but in children with a chromosome disorder can be generally expected to add to the child's difficulties (Ayraud 1976; Higginson 1976; Abuelo 1982; Martin-Pont 1985; Fagan 1989; Morey 1990; Montgomery 2000; Chromosome 7; *Unique*).

■ Palate

Three babies were born with an opening in the roof of the mouth due to incorrect formation during development [cleft palate] but this has not affected any *Unique* members. Among *Unique* members, a broad or high palate is more common. Food can gather in a high palate, so care and frequent drinks are needed at meals (Dennis 1977; Hull 1979; Young 1984; Montgomery 2000; Cheong 2008; Chromosome 7; *Unique*).

■ Eyesight

A number of structural eye and vision problems have been noted. Five babies had glaucoma at birth and two further babies were born with hazy corneas [front of the eyeball] which cleared within days. Congenital [at birth] glaucoma is a problem caused by defective outflow from the front part of the eye due to malformation of the main drainage canal. This results in raised pressure within the eye. True congenital glaucoma occurs during intrauterine life. In addition to hazy corneas and enlarged eyeballs other significant signs include late canalisation of the tear ducts and dislike of light. Any baby or child with glaucoma should be seen by an ophthalmologist.

Other vision problems observed in individuals include small eyeballs; uneven-sized eyes; uneven-sized optic discs [the visible part of the optic nerve]; a small notch or gap in the eye [coloboma] caused by a developmental defect; and strabismus [a squint] (Ayraud 1976; Dennis 1977; Franceschini 1978; Young 1984; Fagan 1989; Morey 1990; Montgomery 2000; Chromosome 7; Decipher; *Unique*).

“A blood vessel in her right eye haemorrhaged, leaving the vision in that eye impaired. She now wears glasses for computer/school work and has regular eye tests and an eye hospital appointment once a year - 11 years

“Focusing difficulty when younger but has resolved - 11 years

■ Hearing

Hearing problems are not common in children with a 7q21q32 deletion. Two young babies were suspected of being deaf but the diagnosis was only confirmed in one who died very young. Among *Unique* members, the most common problem was glue ear, especially up to age 5, which occurs frequently in all children, causing a fluctuating temporary form of hearing loss. One *Unique* family with an older child of 11 noted high sensitivity due to sensory defensiveness. One adult with a 7q22.1q31.1 deletion had narrow auditory canals but no mention of hearing loss (Martin-Pont 1985; Morey 1990; Decipher; *Unique*).

“Her glue ear is coming back as her grommets are out. Her hearing is at the lower end of normal but fluctuates. She has hearing support and hearing aids but won't keep them in - 6 years

7q31q32 deletions

There is a group of people with a deletion from bands 7q31-q32.

Learning

So far, everyone we have information on has experienced some need for additional support with learning. Most often the extent of learning difficulty isn't stated, but where it is, it is moderate. However, variation in severity of learning difficulty is the norm for chromosome disorders. So while it makes sense to anticipate a need for extra learning support, you will only discover how well your child can learn once s/he is well-supported in a structured, suitable learning environment. Children with delayed motor skills are likely to face difficulties in writing. Where the *FOXP2* gene is deleted from 7q31.1, speech and language is likely to be an especially difficult learning area (Decipher; Chromosome 7; *Unique*).

“ He can just write the first three letters of his name - 10 years

Speech and language

Individuals with a 7q31q32 deletion who have lost the *FOXP2* gene at 7q31.1 are at risk for developmental verbal dyspraxia [see page 6].

“ No sounds that require lip closure or tongue placement. She communicates by crying, with facial expressions, by reaching and pointing, with some vocal noises and one sign for 'eat' - 2 years 5 months

“ He understands an awful lot more than he can convey or we know. He has a very sing song voice and is always vocal even when playing on his own but he has difficulty forming sounds with his lips, so many words sound like 'Daaa'. In the last year he has started saying words more clearly but with the communication aid you can have a conversation and on the computer he can achieve so much more - 10 years

Sitting, walking, running

Children are typically late to reach their mobility milestones, rolling from around 7 or 8 months, sitting by their first birthday and starting to walk later than 18 months. Once on their feet, some children have an awkward gait and may be unsteady. In at least two children, the tendons in the legs were tight so they tended to walk on their toes. One child was diagnosed with cerebral palsy and another had repeated casts, Botox injections and surgery to slacken the tendons (Sarda 1988; Decipher; *Unique*).

Muscle tone

Muscle tone may be low [hypotonia], making a baby feel floppy to hold. In one child tone in the trunk was low, while muscle tone in the arms and legs was high [hypertonia]. Tone usually improves

Sources and references

Information comes from 48 cases: 12 in the published medical literature, 6 from *Unique*'s database; seven cases from the Chromosome 7 database (www.chr7.org); and 23 unpublished cases from the Decipher database.

Information varies from full developmental and medical data to a handful of salient features. So it's possible that some important information has been missed out, especially as regards development after babyhood and early childhood (Sarda 1988; Feuk 2006; Bucan 2009; Decipher; Chromosome 7; *Unique*).

with maturity and physiotherapy; some children will need orthotic supports while they are learning to stand and walk (Sarda 1988; Chromosome 7; Decipher; *Unique*).

Using their hands – fine motor control

“ Slight fisting of hands until 1 year old. Voluntary release (putting object in box) at 26 months. Pincer grasp emerging at 27 months. We have used brushing therapy. She still has trouble with aim, ie releasing shape into shape sorter at the right time
- 2 years 5 months

Behaviour

Individuals with a 7q31q32 deletion can have a range of unusual behaviours, including a short attention span, unusual sensory issues and hyperactivity. Autistic spectrum disorder [ASD] characteristics have been observed. ASDs are characterised by disturbances in social behaviour and impaired communication as well as repetitive behaviours and/or a narrow range of interests. However, there is no convincing evidence yet that the *FOXP2* gene that underlies the developmental verbal dyspraxia also plays a role in the autism. A separate autism susceptibility locus has been suggested as lying within band 7q31 and in one study of people with autism, a small deletion from 7q31 was found including the *RNF133* and *RNF148* genes (Sarda 1988; Feuk 2006; Bucan 2009; Chromosome 7; Decipher; *Unique*).

“ Quick to smile and interested in people. When she is tired, hungry or wants to get out of the stroller, she pulls on her collar, stiffens her body and stares blankly until she falls asleep or her needs are met. Seizure activity was ruled out by the neurologist who described these as ‘tonic episodes’ - 2 years 5 months

“ He has a very loving nature but can be over-friendly, wanting to kiss total strangers. He has no concept of danger or nastiness. He has little understanding of time and cannot wait. He gets very impatient and upset and can have a screaming tantrum over a very little thing and can take a while to calm down - 10 years

Sleep

“ He has always had restless nights. He thrashes about and makes a lot of noise, wakes himself up, falls out of bed and crashes about going to the toilet in the dark - 10 years

Feeding

Early feeding difficulties are very common among newborn babies with a chromosome disorder. Difficulties are not mentioned in the medical literature or on Decipher or the Chromosome 7 database, although one child has numerous food allergies. The evidence from *Unique* is that early difficulties may last only a few days and breastfeeding can be successful. However some babies have poor control of the muscles in their mouth, making feeding slow, difficult and messy. Coordinating sucking with swallowing may be difficult and reflux [where the feeds return up the food passage] has occurred, requiring thickened feeds, careful positioning and sometimes anti-reflux medication (Chromosome 7; *Unique*).

“ At risk for aspirating liquid consistencies. Started OT at 14 months to address oral motor control – excessive drooling and gagging on thin liquids - 2 years 5 months

Growth

Three/5 babies were small for dates at birth. Five children are known to be short for their age, one is average height, one is thin and tall and one is thin (Sarda 1988; Decipher; *Unique*).

You may notice

■ Hands

Some slightly unusual features of the hands are quite common in chromosome disorders and most are not specific to a particular disorder or syndrome. Among individuals with a 7q31q32 deletion, stubby thumbs, short middle finger joints and incurving fifth [little] fingers have been observed, as has a tendency for the nails to grow very fast. A more serious problem was seen in one baby with a tiny deletion from band 7q31.33 whose thumbs and radius bones [the shorter, outer bone in the forearm] were underdeveloped or missing (Sarda 1988; Chromosome 7; Decipher; *Unique*).

■ Feet

One baby was born with club feet. Club foot [talipes] occurs more commonly in babies with a chromosome disorder than those without. While it is sometimes specific to the child's particular chromosome change, often it is not. Treatment, individually tailored, aims to straighten the foot so that it can grow and develop normally. First-line treatment is non-surgical but surgery is considered if non-surgical treatments are not completely successful (Chromosome 7).

■ Minor genital anomalies

Minor genital anomalies occur more commonly in babies, especially boys, with a chromosome disorder than in typically developing babies. One baby boy was born with undescended testicles, one of which came down spontaneously. If testes do not descend spontaneously, they can be brought down and fixed in the scrotum [orchidopexy] (*Unique*).

■ Facial and teeth

When searching for a diagnosis for a particular baby or young child, geneticists examine and sometimes list facial features that are somewhat unusual. These features usually only matter when they contribute to a 'typical' facial appearance for a particular disorder or syndrome, so that unrelated children can look surprisingly like each other. In the case of 7q31q32 deletions, there is no evidence that such a 'typical' face exists. Features reported in individuals with a 7q31q32 deletion include slow hair growth or sparse hair; a small, triangular face; a high and wide or narrow, receding forehead; thick eyebrows that meet [synophrys]; downslanting or widely-spaced eyes [hypertelorism]; skinfolds across the inner corners of the eyes [epicanthic folds]; low-set ears that may stick out; a small nose; a low bridge to the nose; a bulbous or broad tip to the nose; a long/ short groove [philtrum] between the nose and upper lip; a wide mouth with thick lips; downturned corners of the mouth; a thin upper lip; wide-spaced teeth; soft enamel on some adult teeth (Sarda 1988; Chromosome 7; Decipher; *Unique*).

Clinical concerns

■ Heart

Two babies were born with a heart defect. One had a hole between the two upper

chambers of the heart [atrial septal defect/ASD]; the defect in the other baby was unspecified (Chromosome 7).

■ Seizures

Six babies or children have had seizures. Generally, the type of seizure is not known but one child had febrile seizures [with a high temperature]; another had focal seizures, once known as partial or complex partial seizures, where the abnormal electrical activity starts on one side of the brain; in a third child, seizures started at 18 months but were controlled with anti-epileptic drugs and at the age of 10 the child had been seizure-free for two years (Chromosome 7; Decipher; *Unique*).

■ Head and brain

Three children had a small head [microcephaly]. In two, the head was unusually short from front to back [brachycephaly]. Two further children had plagiocephaly, where the head looks like a parallelogram when seen from on top. In another child, the joints between the bony plates of the skull had fused too early, creating a condition known as craniosynostosis. Depending on which bones join too early, the brain assumes an unusual shape. To allow the brain more room to grow, a surgical operation known as a craniotomy may be performed to separate the bone plates in the skull.

We only have information on one child who had an MRI scan of the brain. This revealed late myelination [insulation of the nerve fibres; myelinated nerves conduct impulses faster]. Measurements of the electrical activity of the brain [electroencephalogram/EEG] were normal and this child did not have seizures (Sarda 1988; Decipher; *Unique*).

■ Respiratory infections and general wellbeing

There is evidence from *Unique* that some babies and young children suffer frequent and severe respiratory infections. This may be due in part to a delayed ability to cough up secretions (see page 6) and in part to aspiration from reflux (see page 10). One baby was born with hypothyroidism (Chromosome 7; *Unique*).

■ Palate

Two babies were born with an unusually high palate. This, together with difficulties in moving the muscles of the mouth and throat, can cause food to gather at the top of the mouth (Sarda 1988; Decipher).

■ Eyesight

Two children have a squint [strabismus], usually treated with patching, exercises, glasses to correct a refractive error such as long sight and/or surgery to realign the muscles that hold the eye in place. Two children are short sighted, although one child has one eye that has short sight and one that has long sight. Two children have a disorder of the upper eyelid known as ptosis. The eyelid droops so the eye is not fully open and children may tilt their heads back to see properly. If ptosis interferes with vision, the eyelid may be lifted in a surgical operation. Two children have the involuntary eye movements known as nystagmus (Decipher; *Unique*).

■ Hearing

Frequent ear infections and the build-up of a sticky fluid behind the eardrum known as

glue ear is common in young children and may be particularly common in children with chromosome disorders, observed in at least half of *Unique* members. Glue ear causes a temporary, fluctuating hearing loss and treatment for a child whose hearing is substantially impaired involves inserting tiny plastic aeration tubes [grommets] into the eardrum. As children grow and the channels leading from the middle ear become more vertical, glue ear tends to improve on its own. Just one child has been diagnosed with a permanent hearing loss in both ears (Chromosome 7; *Unique*).

Why did the chromosome deletion occur?

A blood test to check both parents' chromosomes is needed to find out why the 7q deletion occurred in the child. Most 7q interstitial deletions occur when both parents have normal chromosomes. The term that geneticists use for this is **dn**, short for 'de novo', meaning 'a new event'. Dn 7q deletions are caused by a sporadic mistake that is thought to occur when the parents' sperm or egg cells are formed or very soon after fertilisation [see page 3].

No environmental, workplace, dietary or lifestyle factors are known to have caused these chromosome changes. What is certain is that as a parent there is nothing you did to cause the break to occur and nothing you could have done would have prevented it from occurring in your baby. No one is to blame when this occurs and nobody is at fault and there is no reason for anyone to feel guilty.

Can it happen again?

The possibility of having another pregnancy with a 7q deletion depends on the parents' chromosomes. When both parents have normal chromosomes, the deletion is very unlikely to happen again.

If either parent has a chromosome change involving 7q, the possibility is greatly increased of having other affected pregnancies. If they wish, parents should have the opportunity to meet a genetic counselor to discuss the specific recurrence risks and options for prenatal and preimplantation genetic diagnosis (PGD). PGD requires the use of in vitro fertilisation and embryo biopsy, and only healthy embryos are transferred to the mother's uterus. If the parents choose to conceive naturally, prenatal diagnosis options include chorionic villus sampling (CVS) or amniocentesis to test the baby's chromosomes. Testing is very accurate, although not all of these tests are available in all parts of the world.

Could my child with a 7q deletion have similarly affected children?

In any pregnancy, someone with a 7q deletion is likely to have a 50 per cent risk of passing it on and a 50 per cent chance of having a child without it. If the deletion is passed on to a second child, it is likely that he or she will have characteristics similar to the first child but there could also be significantly different clinical presentations for the reasons described earlier.

Support and Information



Two girls, each
with a
7q22.1-31.2
deletion:
Above left
- 10 years
Right - 14 years



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Facebook group for 7q deletions and duplications:

www.facebook.com/groups/493223084038489

Unique lists external message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

This information 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. The guide was compiled by Unique and reviewed by Dr Steve Scherer, Centre for Applied Genomics, Hospital for Sick Children, Toronto, Canada and by Professor Maj Hultén, BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, 2011.

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