Support and Information

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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 Maria Cristina Digilio, Medical Genetics Unit, Bambino Gesu Hospital, Rome, Italy and by Professor Maj Hultén, BSc, PhD, MD, FRCPath, Professor of Medical Genetics, University of Warwick, 2005.

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Duplications of 8q

Sources

The information in this leaflet is drawn partly from the published medical literature.
For references to articles, the first-named author and publication date are given to allow you to look for abstracts or original articles on the internet in PubMed.

The leaflet also draws on Unique's database. At the time of compiling the information, Unique had 35 members with an 8q duplication, seven with a pure duplication of 8q not involving any other chromosome. Fifteen families completed a detailed questionnaire in 2004/5. References to information from the Unique database and the questionnaire are marked U. Unique is extremely grateful to the families who provided information about their child's progress.

8q duplications

8q duplications are rare genetic conditions. They are caused by having extra material from one of the body's 46 chromosomes. Generally speaking, having extra chromosome material increases the risk for problems such as birth defects and growth and developmental delay. With 8q duplications the picture depends on what chromosome material is duplicated and whether any other material has been lost.

Chromosomes are the microscopically small structures in the nucleus of the body's cells that carry genetic information. They are numbered in size order from largest to smallest, from number 1 to number 22. We usually have two of each chromosome, one inherited from our father and one from our mother, in addition to the sex chromosomes (two Xs for a girl and an X and a Y for a boy).

Each chromosome has a short (p) and a long (q) arm. People with a chromosome 8q duplication have a repeat of some of the material from the long arm of one of their chromosomes 8. The other chromosome 8 is the usual size. Large 8q duplications are sometimes also called trisomy 8q or partial trisomy 8.

Frequent features

- Developmental delay.
- Some degree of learning difficulty.
- Heart conditions. These may be simple but are more often complex and need surgical correction.
- Problems with the bones and joints, specifically missing or extra ribs, absent or small kneecaps.
- Anomalies of the genitals and/or urinary system. In boys, this may include undescended testicles, a small penis and perhaps a small scrotum. In girls, anomalies are more likely to be internal and may include a partial division of the uterus into two horns (bicornuate uterus).
- Cosmetic similarities. These can include large ears, a horizontal crease below the lower lip, a 'pouting' lower lip, a short neck that allows the chin to rest direct on the chest.
- Similarities of body build. These can include widely spaced nipples, a long slender upper body with sloping shoulders, a hollowed chest (pectus excavatum) and spinal curvature.

(Fineman 1979; Walker 1987; Kozlowski 1988; Gelb 1991).

place with the short arm of any other chromosome or with the long arm of any chromosome, it is possible that there will be additional effects caused by material lost from that chromosome. There are many examples in this leaflet of children with an 8q duplication and material lost from a different chromosome. Ask your geneticist about this.

A parent with a **pericentric inversion** has one chromosome 8 in which two breaks have occurred, one in the short arm and one in the long arm. When eggs or sperm are formed, the risk is that the chromosome 8 with the inversion will give rise to a baby with unbalanced chromosomes, typically involving a duplication and a deletion.

In all inherited cases, the risk of having another affected pregnancy is significantly increased. Families can discuss their individual situation with their genetics service.

When it's not inherited

When tests show that the parents' chromosomes are normal, the duplication has almost certainly arisen as a chance event. Geneticists call this *de novo*, meaning that the affected child is the first person in the family with the chromosome disorder. It is then extremely unlikely to happen again. There is a very distant possibility that in some people the duplication occurred during the formation of the cells that later give rise to the egg or sperm. This can result in a mixture of normal and abnormal egg or sperm cells (gonadal mosaicism or germline mosaicism), with a real chance of another affected pregnancy. However, the chances of this happening are very small indeed.

" He loves books, turns the pages and likes to touch and feel them. He has a great smile and laugh - he is very happy and full of a joy that is contagious. He's affectionate and loves people -
age 2, duplication of 8q24.2 with a deletion of 9p24.

an 8q11- q13 duplication, firm breast tissue was noted at 8 months and a tentative diagnosis of precocious puberty was made. In a boy with a mosaic 8q11.23 - q22.3 duplication, puberty proceeded normally from the age of 15 years (Sujansky 1993; U).

Behaviour

Unique has no evidence of a specific effect of 8q duplications on behaviour. Children who cannot communicate their needs may express frustration in any of a range of behaviours well known to any experienced parent, notably tantrums, screaming, throwing themselves to the floor, biting themselves and throwing. Two families noted that their child's behaviour was negatively affected by constipation (U).

Will a child ever be able to live independently?

There is no clear pattern that is typical for all. It is highly likely that people who are minimally affected by their chromosome disorder will be able to live independently. However, among *Unique*'s membership, no-one is so mildly affected.

Unique's oldest member with an 8q duplication is 18 years old. With a mosaic form of the disorder, he is relatively mildly affected. He lives at home and, with a support worker, follows college courses in woodwork and computers. His leisure activities include swimming, going to the gym and attending clubs for people with special needs. He needs a high level of supervision and has a social worker and the support of his family.

Among children who are more severely affected, the typical delay in self care skills including toileting, feeding and washing means that it is unlikely that they will ever achieve full independence.

Causes

To answer the question 'Why did this happen?' a geneticist needs to know about the parents' chromosomes. In some cases of 8q duplication, it will turn out that one or other parent has a rearrangement of their own chromosomes. Rearrangements occur in chromosomes as part of evolution. They affect children from all parts of the world and from all types of background. They also happen naturally in plants and animals. So there is no reason to suggest that your lifestyle or anything that you did caused the duplication of chromosome material.

When it's inherited

There are two types of typical chromosome rearrangement in the parent that are likely to give rise to an 8q duplication in a baby. In both rearrangements, the parents themselves are usually healthy and have no developmental problems because the correct amount of chromosome material is present.

A parent with a **balanced translocation** has chromosome material switched between different chromosomes. Usually two chromosomes are involved, but it can be more.

If the swap of chromosome material has taken place between chromosome 8 and the short arms of either chromosome 13, 14, 15, 21 or 22, the effects on the baby if unbalanced are most likely to just be of the 8q duplication. If the swap has taken

Other features

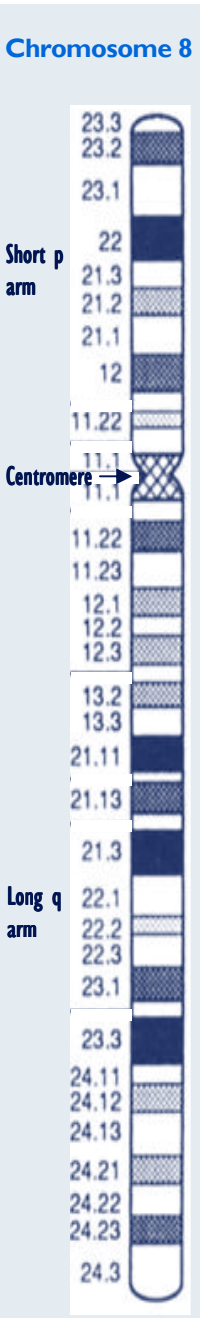
All of the features listed below have been noted in the published medical literature or on the *Unique* database. It is quite possible that some are coincidental findings but the more often they occur, the more likely it is that they are really part of an 8q duplication. Some features only occur when particular segments of the chromosome are repeated, so it is important to know the exact breakpoints. Your child's geneticist or paediatrician can tell you this. In the enclosed notes **Different 8q duplications**, you will find brief notes on particular segments.

- Progressively contracted joints, especially in the lower body.
- Odd angle of feet at birth, prominent heelbone (calcaneus).
- Deep creases in soles of feet and/ or palms of hands.
- Normal birth weight, followed by slow growth in babyhood and childhood, leading to eventual short height.
- Seizures.
- Cleft palate, with or without a cleft lip.
- Blockage of the nasal passages, known as choanal atresia.
- Hair growth on back and trunk.
- Abnormal degree of tone in the skeletal muscles, either increased so that muscles feel taut (hypertonia), or low, so they feel floppy (hypotonia).
- Abnormal tooth development, thick gums.
- Irregular or cleft alveolar ridge (the ridge behind the upper teeth).
- Lungs with two lobes instead of three.

At 12 months. This little boy has an 8q24.2 duplication, with a small deletion of 9p.

How rare are 8q duplications?

No one can be certain because of the numbers of people who might have this duplication but are only very mildly affected by it and are therefore never detected. The number of cases published in the medical literature had reached at least 50 as long ago as 1987, making this a fairly common rearrangement in the world of rare chromosome disorders.



Appearance

Some typical features include wide set eyes, a broad bridge to the nose, a 'pear-shaped' nose with a bulbous tip, a 'pouting' lower lip with a horizontal crease beneath it and large ears. Some children have excess skin on the neck, which is typically broad and short. Some children also have unusual hair growth on their trunk and body. The families of some children with proximal duplications (duplications of material from close to the point where the long arm and short arm meet) have commented on their soft skin. As for body build, narrow, sloping shoulders and a long, narrow trunk with a hollowed chest and in many cases a spinal curvature, most frequently an S or C shaped curve, are typical (Walker 1987; U).

Pregnancy

There has been little formal research into pregnancies affected by an 8q duplication, but in pregnancies with babies with **Recombinant 8 syndrome** where babies have a duplication from 8q22.1 as well as a small deletion from the short arm from band 8p23.1, no consistent prenatal complications were noted.

An 8q duplication does not typically delay growth prenatally. Two features were noted repeatedly in the *Unique* series. Excess amniotic fluid (polyhydramnios) was found in the second half of pregnancy in a pregnancy with a baby with a duplication from 8q11 to 8q13, but ultrasounds were normal and the baby was born at 37 weeks. Polyhydramnios was also detected from the seventh month in a pregnancy with a baby with duplication from 8q22 as well as a 3p25 deletion, leading to the draining of five litres of amniotic fluid. A pregnancy with a baby with an 8q22 duplication and a deletion from 15q26 was described by the mother as 'huge'. Three mothers had raised levels of alpha-fetoprotein in early pregnancy serum screening tests. Other pregnancies were reported as uneventful (Sujansky 1993; U).

Newborn

Much of what is known formally about the course of the newborn period in babies with 8q duplications comes from a 1993 study of the natural history of Recombinant 8 syndrome. In this group, delivery was at term in 24/38 babies and no specific pattern of difficulties was seen. Five of 14 babies with a known Apgar score had a 1-minute score under 5 (Sujansky 1993).

In the *Unique* series, a baby with an 8q11-q13 duplication had repeated apnoeas (where she stopped breathing) and needed supplemental oxygen for the first three days. These were attributed to her short neck which allowed her head to flop forwards and improved when a roll of material was placed under her neck. A baby with an 8q12.2-q22.1 duplication had a weak cry and slept continuously with no desire to feed. A baby with an 8q21.1-q22.3 duplication with a cleft palate needed ventilation support for 13 days.

Among the babies in the *Unique* series with simultaneous chromosome deletions, one baby with a 1p36 deletion who was a twin, was born underweight (2lb 12oz/1247g compared with his unaffected twin's birth weight of 5lb 2oz/2324g) and had difficulties regulating his body temperature (U).

conductive hearing loss, two a permanent nerve deafness, one severe. Only two children had normal hearing. It is suggested that children with this disorder have tubes inserted after the first attack of middle ear infection.

In the *Unique* series, conductive hearing loss was also common. One child with an 8q21.1- q22.3 duplication also had a mild to moderate permanent hearing loss. Among the children who also had deletions, a profound hearing loss in one ear with a mild loss in the other was found in a child with a 1q44 deletion; the anvil, one of the tiny bones in the middle ear, was defective in a child with a 6p25 deletion; and a child with a 9p24 deletion had very narrow external ear canals (Sujansky 1993; U).

Eyesight

A wide variety of defects of vision and eyesight have been noted in children with an 8q duplication. Squint (strabismus) occurs commonly in children with chromosome disorders and may require correction by surgery. It was observed in 5/5 children with a large terminal duplication from 8q21 or 8q23. Ptosis occurs when the upper eyelid cannot be fully raised. If the lid impedes vision, it can be corrected surgically. It has been observed in children with both small and large duplications of 8q.
Vision anomalies were seen in more than half the children with Recombinant 8 syndrome. After strabismus, nystagmus (rapid, involuntary eye movements) and short or long sight were observed most frequently.

In the *Unique* series, one child with an 8q12.2- q22.1 duplication was observed with abnormal development of the optic nerve but unaffected vision; a child with an 8q24.1 duplication and a 2q32 deletion who was sensitive to bright light was observed to have a thin retina; and a child with an 8q24.2 duplication and a 9p deletion also had underdevelopment of the optic nerve and unusually small eyes (Walker 1987; Sujansky 1993; U).

Puberty

Published experience with puberty in children with 8q duplications is limited. In children with Recombinant 8 syndrome, in five girls over 10 the onset of puberty was known to be normal. In one girl, periods started at the age of 9 and ceased by age 15. In the *Unique* series, in a girl with

> " She loves videos, TV and playing hide and seek. She knows how to dress herself, eat, drink and set the table and plays well with her dolls and toys. She is also very determined, laughs a lot and observes others.
>
> " Most of the time she is very happy and she understands many, many things. We have gained patience and take nothing for granted
>
> - age 5, 8q21.1 - q22.3 duplication.

children had deep creases in the soles of their feet or the palms of their hands, but these typically become less obvious with age (Walker 1987; U).

- Genital area, reproductive tract and bottom

Typically, boys with an 8q duplication are born with undescended testicles and sometimes a small penis or scrotum. In girls, visible anomalies are less common, although as many as one girl in three may have small labia (external skinfolds) or a small or large clitoris. In girls, the hole for the bottom (anus) may also be close to the vagina. In one girl there was a connexion between the vagina and the rectum. A two-horned (bicornuate) uterus has been repeatedly observed.
Structural anomalies of both the kidneys and urinary tract affect at least half of all babies with an 8q duplication. The anomalies of the urinary tract may make urinary reflux more likely, so that antibiotic protection will be given (Walker 1987; Kleczkowska 1991; Sujansky 1993; Vianna-Morgante 1996; U).

- Seizures

Half of children with Recombinant 8 syndrome have been shown to develop seizures, in most before school age and in one at the age of 14. All children responded well to antiepileptic medication. In the *Unique* series, seizures were less common and were well controlled with medication (Sujansky 1993; U).

- Joints

Contracted joints have been noted in 6/8 children with an 8q duplication, typically developing after babyhood. In children with Recombinant 8 syndrome, major joint contractures developed most often after the age of 10 and usually affecting the lower body. Although three children had corrective surgery, none showed an improvement and two became wheelchair dependent. In the *Unique* series, hip laxity has been noted in babies where the socket of the hip joint is shallow. In a few children some hip tightness has been noted but only one child, aged 8, has a history of progressively contracted joints (Walker 1987; Brueton 1992; Sujansky 1993; U).

General health

A high rate of post-surgery complications has been noted in children with Recombinant 8 syndrome, suggesting that alternative approaches should be considered first. This has not been seen in the *Unique* series of children with a wide variety of 8q duplications (Sujansky 1993; U).

Teeth

10/11 children with Recombinant 8 syndrome had dental anomalies, most often widely spaced teeth. Two children had notches in the alveolar ridge just behind the upper front teeth. The *Unique* series showed a broader range of dental anomalies, including crooked and missing teeth, an extra tooth in the upper jaw, deficient enamel of the front teeth leading to early decay and very small, 'transparent-looking' teeth. Milk teeth were sometimes late to fall out (Sujansky 1993; U).

Hearing

11/15 children with Recombinant 8 syndrome had a hearing loss, nine a bilateral

Growth

Babies with Recombinant 8 syndrome have a head circumference, weight and length at birth that are normal but by the age of four months all have growth delay. Among babies with other 8q duplications, average birth weight in a series of 22 babies was 6lb 11oz/3026g and slow growth and failure to thrive were seen in 24-28 out of 38 babies. In the *Unique* series, the range of birth weight among single born babies with a pure duplication was 5lb15oz-7lb1oz/2494-3210g and among those with an additional deletion it was 1814-3900g/4lb-8lb10oz. Many children with an 8q duplication are tall and slim, but not all. Children with additional deletions were in general shorter (Walker 1987; Sujansky 1993; U).

Feeding

Failure to thrive is especially severe in the Recombinant 8 babies because of the large numbers with severe heart defects. The *Unique* series had more babies with a cleft palate and fewer with severe heart defects.

Feeding difficulties were universal in the newborn period, with babies sucking too weakly to meet their own needs, making breast feeding impossible. Typically, new babies needed nasogastric tube feeding for one or two weeks (the tube is passed through the nose and down to the stomach) and one baby was fed through a gastrostomy tube direct into the stomach. One baby had severe gastro-oesophageal reflux (where stomach contents flush readily back up the food pipe due to poor action of the valve that closes the food pipe off from the stomach) that responded reasonably to thickeners added to formula but poorly to medication.

By the age of two or three, children were typically eating a good variety of everyday family foods and drinking from a spouted cup or bottle. Among children with additional chromosome deletions, the feeding difficulties proved generally more persistent due to low muscle tone in the face and mouth (with difficulties chewing, swallowing and retaining food). Children were more liable to have severe reflux and to aspirate their feeds, and while one child outgrew this by the age of five, others were more likely to need a surgical operation (a fundoplication) to improve the action of the valve at the entrance to the stomach, or the insertion of a long-term gastrostomy tube. One child with a small duplication from 8q24.2 and a deletion from 9p24 fed successfully.

Constipation

Constipation is common in children with chromosome disorders and families need to be inventive in finding ways for their children to take enough fluid and fibre. Most families use stool softeners and some also use stimulants as enemas or suppositories.

> " Alana suffered severe reflux until 9 months and no medications helped. Finally we went to a kinesiologist and within a day the reflux had stopped.

> " He had initial feeding difficulties and was hospitalised due to dehydration but I breastfed exclusively for three months, supplementing with formula by syringe. He then had breast milk and formula to 10 months, and at the age of 18 months eats very well and loves most food and drinks with a straw.

How can this affect learning?

People with 8q duplications are generally said to have a mild to moderate learning difficulty and there are reports of people with little or no learning difficulty. A 5 year old boy with a duplication of 8q13 - q21.2 has been described with normal learning ability. A large family with many members with a duplication from 8q21.2- q22 showed a range of learning ability, with some family members in employment.

A girl with a duplication from 8q24.11- q24.3 only came to medical attention because of borderline learning difficulties at the age of 11 and was found to have an IQ of 72 and greater difficulties with hand use and perceptualisation than with speech.

This picture is generally supported by evidence from *Unique*. While some children only appear to have a mild learning difficulty, in others it is more obvious so that a three year old may be operating at the level of a nine-month-old baby. Children were generally sociable and learned by copying others. Their understanding was concrete rather than abstract. Some families reported high functioning speech and language giving a misleading impression of their child's learning ability.

There was no immediately obvious association between the level of learning disability and the amount or position of repeated chromosome material, apart from those youngsters with a duplication at the very tip of the long arm who appeared to be less obviously affected.

However, researchers found that in children with Recombinant 8 syndrome, the developmental quotient fell with age. An initial mild delay therefore did not necessarily predict mild disabilities in later childhood. Two children nonetheless showed exceptional ability in language and movement and the researchers noted that at least one set of their parents was very experienced in dealing with developmental problems.

Among children with involvement of other chromosomes, the picture is more mixed and less predictable. A group of children has been described with mild learning difficulties and a duplication from 8q24.13 as well as a1q44 deletion; this picture is consistent for *Unique*'s member with duplication from 8q21.2 and a 1q44 deletion. A child has been described with a moderate learning delay and an IQ of 51 with a duplication from 8q23 - q24.2 and a deletion from 2q37. In *Unique*'s membership, a child with a duplication from 8q24.1 and a 2q32 deletion has a severe learning disability (Bowen 1983; Romain 1989; Kleczkowska 1991; Stengel-Rutkowski 1992; Sujansky 1993; Giltay 1998; U).

"She needs things to be real to reinforce learning. She can be a very happy sociable little girl.

prominent and in one *Unique* member with an 8q21.1- q22.3 duplication, the bony structure of the left heel was abnormal. Toes are often crooked and there may be a 'sandal gap' between the first and second toes. In the hands, the fingers in babies may not be able to be fully straightened and the fifth finger may curve inwards. Evidence from *Unique* suggests that in some children clenched fingers straighten in childhood. One *Unique* member with a duplication from 8q12.2- q22.1 has fragile bones and broke a femur at 3 months (Walker 1987; Kozlowski 1988; Kleczkowska 1991; Sujansky 1993; U).

Spine

The natural history of spinal curvature has been well studied in the Recombinant 8 syndrome, where nine out of 11 children had a spinal curvature. The youngest child in whom it was seen was aged 4. No underlying vertebral anomalies were seen and the curve was neuromuscular in origin. It tended to deteriorate and in older children required bracing or surgical correction (Walker 1987; Sujansky 1993).

In the *Unique* series, 40 per cent of children had a spinal curvature. In early to middle childhood, the degree was not severe, requiring no more than monitoring in some children, while others needed bracing. In one child who received chiropractic the degree of curve improved from 23 degrees at age 5 to 11 degrees at age 7 (U).

Mouth

Most children with an 8q duplication either have an unusually high roof to the mouth (a high arched palate) or a split in the palate or the finger-like projection of tissue that hangs down at the back of the mouth (a cleft palate or bifid uvula). Tongue tie also occurs, caused by a short and typically thick frenulum, the tissue that attaches the tongue to the floor of the mouth. This can be treated by clipping. The frenulum that attaches the upper lip to the gum may also be short and thick. A marked narrowing or blockage of the nasal passages (choanal atresia) has also been repeatedly described in children with an 8q duplication, but not in the *Unique* series (Walker 1987; Kleczkowska 1991; Jervis 1993; Sujansky 1993; Vianna-Morgante 1996; U)

Limbs and feet

Most babies with an 8q duplication are born with feet held in an abnormal position. This usually needs surgical correction but physiotherapy and bracing may be enough to mould the feet into a position suitable for walking. Seven out of 15

"She has been an inspiration to us all. Her strength, love and zest for life give her the determination to live each day to the fullest. She is constantly surprising us all and she amazes the doctors. We love her so much.

"She loves playing with her kitchen, being outside and riding her three-wheeler bike. She loves handbags and phones and will laugh at the funniest home videos

- age 3, 8q?13 - q11 duplication.

Medical concerns

Heart

The clinical problem that is most often described in people with an 8q duplication is a heart defect. In one series, 30 babies out of 33 were born with a heart defect. In another series, nine babies out of 20 with a duplication from 8q13-24 to 8qter had a heart defect. In the *Unique* series, they occurred in 16 out of 35 children. However, of these 16 babies, six needed no surgery and the defect, usually a small hole between the upper or lower chambers of the heart, was allowed to close naturally. The typical heart defect in babies with 8q duplications is known as a conotruncal defect. It occurs in as many as two thirds of babies with Recombinant 8 syndrome. Conotruncal defects arise five to six weeks after conception when the heart is still an S-shaped tube with upper and lower bulges. A dividing wall called the conotruncus divides the lower heart area into what will become two ventricles (pumping chambers) and two major arteries, the pulmonary artery that leads to the lungs and the aorta that leads to the rest of the body. A defect in the conotruncus causes incorrect circulation of oxygenated and depleted blood.

The most common types of conotruncal heart defect are:

- Double outlet right ventricle, where the aorta and pulmonary artery both arise from the right side of the heart.
- Pulmonary atresia, where a narrow valve at the entrance to the pulmonary artery blocks blood flow to the lungs.
- Tetralogy of Fallot where the right heart is underdeveloped, there is a hole between the ventricles, the pulmonary artery is underdeveloped and the aorta is overriding.
- Transposition of the great vessels where the main blood vessels leading from the heart are reversed.
- Truncus arteriosus where a single blood vessel replaces the pulmonary artery and aorta.

Correcting a conotruncal defect requires complex surgery and you will be given an opportunity to discuss the full implications of this with your baby's doctors.
(Fineman 1979; Walker 1987; Gelb 1991; Sujansky 1993; Digilio 2003; U)

> " A had a large VSD and a small ASD and went into cardiac failure prior to surgery. At the age of three months, she had major heart surgery, the large defect was closed with a patch and the small defect was stitched. Today, at the age of 3, she is monitored but has no problems whatsoever - 8q11- q13 duplication.

Skeleton

8q duplications appear to affect the development of the skeleton in specific ways. The kneecaps are typically small, thin or absent. The trunk area is usually slender and the shoulders are sloping. In some children the top two pairs of ribs are small and undeveloped and there may be a gap in these ribs. There may be an extra thirteenth pair of ribs. Over time, the chest may become hollowed in a formation known as pectus excavatum. In the pelvis, the hip sockets may be shallow. The vertebrae may be abnormally formed. In the feet, the heelbone is also unusually

Learning: schools and families say …

> " A steadily displayed good progress in playgroup and her skills and abilities improved to allow her to progress to a general playgroup session. She has made an amazing transition. She attends well to tasks, perseveres when difficulties are encountered, really enjoys dramatic play activities, matches shapes and colours, understands comparisons, can complete 6-9 piece lotto matching boards and 6- 8 piece inset jigsaws, listens to a short story read to her, is starting to imitate lines and a circle. She displays great pleasure in her own achievements - 8q11 - q13 duplication, age 2y 9m.

> " A has moderate learning difficulties and needs things to be real to reinforce learning. She can read some simple words and identify and name about half the letters of the alphabet and do very simple mathematics. However, her listening skills are poor and even though she has no hearing problem she cannot identify words beginning with the same sound – duplication from 8q24.13 with 3p26.2 deletion, age 7.

> " H performs like a 5 year old. She can count to 10 but cannot write, loves to colour, do puzzles or any craft activity. She needs 1:1 or small group teaching as a large group would distract her – duplication from 8q22 with 3p25 deletion, age 8.

> " J's learning difficulties are at the top end of severe. He is very poor at writing, but is socially far more able than would be expected from his academic ability. He reads at a 6-year-level and although his writing has seen a big improvement since the age of 16, his writing and spelling are at a lower age. He still has difficulty with numbers and counting, but he knows what he wants and has good ideas. His strengths are that he is very caring and very strong minded and what helps him is looking up to more able young people - mosaic 8q11.23 - q22.3 duplication, age 18.

Recombinant 8 syndrome is a combination of a duplication of the end of 8q from 8q22.1 and a deletion from 8p23.1.

Recombinant 8 syndrome is also known as San Luis Valley syndrome and is found mostly but not exclusively in the Americas in people of Hispanic origin.

> " A very loving, happy boy. A pure delight to our family who taught us unconditional love.

> " Patience and humour are the keys to success.

Speech and communication

Speech and language are typically delayed and there is some evidence that understanding outstrips expression. In children with Recombinant 8 syndrome, significant degrees of hearing loss were found to impact on speech development. Even children with no hearing loss responded to the early introduction of sign language with improvements in communication and behaviour (Sujansky 1993).

All children in the *Unique* series benefited from using sign language and pictures to stimulate communication before words emerged and signing remained an important communication tool for most children. Most children spoke unclearly and one family investigated the use of a speech-generating device.

Evidence of understanding outstripping speech was found in a child of two years who understood both home languages but communicated by gesture and the use of a single word. A 16-year-old with a mosaic 8q11.23 - q22.3 duplication was described with verbal dyspraxia and some inclarity of speech, but unimpaired understanding. However, in a child with an 8q12.2 - q22.1 duplication, understanding was also severely delayed.

“ He understands some familiar words such as bye bye, time to eat, night night, no no. He can express his likes by smiling and his dislikes by his expression. His progress in speech and communication has been very delayed. We have not yet found a good way to communicate with him. His desire to learn to communicate has not really been there – age 3.

“ More words are coming daily, although he misses the articulation on a lot of them, but he sings happy birthday in tune! - 8q21.2 duplication with 1q44 deletion

“ - age 4, with hearing loss.

“ He has no speech, normal hearing and understands everything, easily following simple and two-part commands and responding appropriately to information. Since the age of 6, he has used a communication device with an electronically generated voice output and sign language modified due to his limited fine motor skills. These have greatly reduced his frustration and given him a better quality of life - age 15, Recombinant 8 syndrome.

Brothers aged 6, 4 and 3, the three -year-old with a duplication from 8q12.2 to q22.1.

“ He loves music, people, loud toys and toy cars. He is a very happy child.

Sitting, moving, walking

The age at which babies learn to hold their head steady and sit up is likely to be significantly delayed, as are the later milestones of moving by scooting, rolling or crawling and then walking.

Hypotonia (low muscle tone) is common and may be severe. It has been observed specifically in the upper body and the truncal area and some children are helped by wearing a supporting lycra vest. Physiotherapy is needed and most children need a standing or walking frame to achieve independent walking and may also need splints or braces for their feet and ankles.

On average *Unique* babies rolled over at 8 months (range 6-12 months) and sat up at 18 months (range 10 months to 2 years and 10 months). They crawled at 21 months (range 12 months to 3 years, 10 months) and walked at 28 months (range 18 months to 3 years). Climbing stairs followed, with most children achieving this before school age. Despite the initial delay, by around the age of 5, children in the *Unique* series were mobile and in some cases, running, jumping and climbing.

Among the children with additional chromosome involvement, the picture was more diverse and two children were reported to have markedly increased muscle tone, making the body unnaturally stiff. One mother was taught infant massage to help her baby relax. Rolling was achieved by 10 months (range four to 24 months), sitting by 14 months (range six to 24 months), crawling, scooting or commando crawling by 18 months (range 12 to 36 months) and walking by 40 months (range 16 months to 5 years). A number of children could not walk without the support of a frame or rollator or manoeuvre themselves into a position for walking without help.

“ At 2 he could walk unaided but was still clumsy and fell over a lot for many years.

“ J does a funky roll, sit up and turn to get around, but uses a wheelchair, prone stander and walker at school – age 41/2.

“ A’s skills are immature, she appears awkward and unsteady when she runs, can achieve small jumps but has difficulty negotiating steps unless they are clearly marked or familiar - age 7.

Using their hands

The *Unique* series showed a possible disparity between children’s fine motor skills (hand use) and gross motor skills (whole body movements). Fine motor skills were almost age appropriate in a few children, while all children showed a marked delay in gross motor development. There was a tendency to delay in using both hands together but most children achieved this by 18 to 24 months. In one child with a deletion from the short arm of chromosome 3, correction of a vision problem improved co-ordination and hand use, but she had no consistent hand grip at 7. However, this picture was not consistent and a teenager with a mosaic duplication of 8q11.23 - q22.3 had severe co-ordination problems and dyspraxia. So long as tasks were broken down into components, he could learn them but at 18 could not tie laces. An 11-year-old girl has also been described with specific fine motor delay (Kleczkowska 1991; U).