2q37 deletions

Unique hosted the first-ever international meeting for families with a child with a deletion from the long arm of chromosome 2 with a breakpoint at 2q37 in Oxford, United Kingdom in June 2010. The meeting brought families from Australia, Dubai, Ireland and all parts of the United Kingdom together with researchers, interested doctors and therapists.

Unique has around 100 members with a 2q37 deletion; the most frequent breakpoint is at 2q37.3, then 2q37.1, and the least frequent is 2q37.2. The great majority of members have a terminal deletion that includes the end of the chromosome. A handful of members have an interstitial deletion within the 2q37 band. Most members have a 'pure' 2q37 deletion, but 19 have a deletion from chromosome 2q37 as part of a wider chromosome imbalance, typically an unbalanced translocation. Twenty-one families and their children met professionals including a paediatrician, geneticists, psychiatrist, computational biologist, speech and language therapist, sleep counsellor, clinical psychologist in training and a clinical nurse specialist with an interest in behaviour in children with special needs. Families heard specific presentations on 2q37 deletions and general presentations on topics of interest to a family with a special needs child.

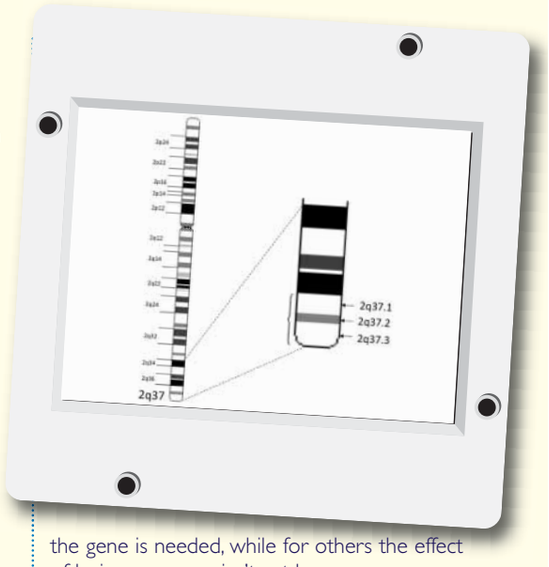
Unique's 2q37 deletions weekend was the fourth in a series of five disorder-specific weekends: 4q deletions; Kleefstra syndrome (9q34.3 deletions); 8p23 deletions and inverted duplication and deletion of 8p; and Pallister-Killian syndrome completed the series. Financial support from Jeans for Genes and the Grocers' Charity was provided for the series of syndrome-specific meetings.

2q37 deletions, a clinical perspective

Dr Louise Wilson, consultant clinical geneticist at Great Ormond Street Hospital, reviewed what is known about people with a 2q37 deletion.

People with a 2q37 deletion have one normal chromosome 2 while the other copy has a small section (band q37) missing from one end. The 2q37 region is subdivided into three bands: 2q37.1, 2q37.2 and 2q37.3 and the missing section can include any or all of these bands (above, right).

In the past very small deletions could be missed but today a technique known as array CGH can identify tiny missing or extra pieces of chromosome material. Array CGH gives a very exact picture of what is missing and even a list of the missing genes. Within the deletion only a minority of missing genes are likely to cause problems: for others only one copy of the gene is needed, while for others the effect of losing one copy isn't yet known.



In 95 per cent of people the 2q37 deletion will be a new event, called *de novo*, and the parents' chromosomes will be normal. When the parents' chromosomes were being copied to pass on in the egg or sperm that went to form the child, a bit went missing just by chance. This means that the deletion only affects the one child; the chance that brothers and sisters will be affected is very small (less than 1%) and there should be no genetic implications for the wider family. In the remaining five per cent of families, one of the parents has a rearrangement known as a translocation between one chromosome 2 and another chromosome. Just by chance the tip of

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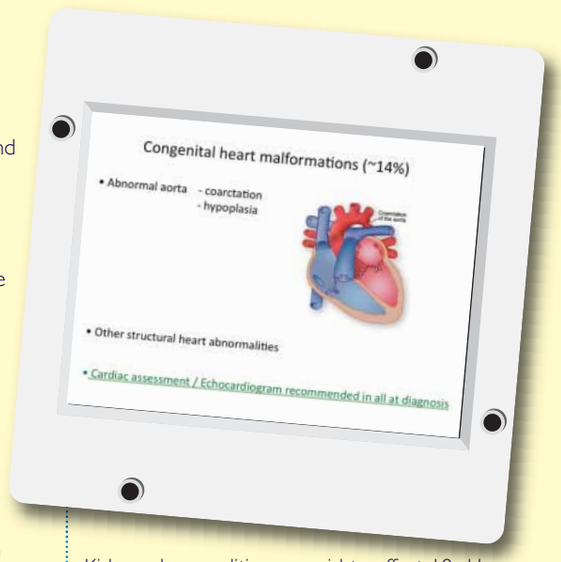
chromosome 2q37 is located on another chromosome and the end of the other chromosome is located on chromosome 2. This doesn't usually cause a problem in the parent, as long as the parent has 2 copies of each gene. But when the parent passes on their chromosomes, there's a risk they'll pass on the chromosome 2 with the translocated tip and the child will have both a 2q37 deletion and an extra part of the other chromosome involved. That extra part confuses the clinical picture so Dr Wilson's talk focused on those with a 'pure' 2q37 deletion (2q37-).

Taking information published in the medical literature, the problems people with 2q37 deletions are likely to encounter are these: early on, low muscle tone leading to floppiness and feeding problems. Around one child in three has a malformation of an organ such as the heart. Later on, mild to moderate developmental delay is likely to emerge. The joints may also be loose. Adults tend to be a little shorter than expected in their family; they tend to gain weight easily. Some have short bones in the hands and feet. More than expected have autism or an autistic spectrum disorder (ASD). Some go on to develop epilepsy. Many of these symptoms are also found in other chromosome disorders and are not specific to 2q37. The short bones in the hands and feet are more unusual and can suggest the diagnosis.

The low muscle tone can contribute to feeding difficulties, causing weak and poorly coordinated sucking and slow early weight gain, as well as delay in gaining head control and in rolling, sitting and walking. This gradually improves with time, physiotherapy and occupational therapy help and children generally learn to walk.

Reflux – bringing back part of the feeds and stomach acid – is common. In some children the valve at the entry to the stomach isn't working properly or there is a hiatus hernia, where part of stomach bulges through the diaphragm, affecting the efficiency of the valve. Reflux can be treated with medication or thickened feeds, but some children need surgery. Reflux usually improves with time and moving on to solids also helps.

Up to 27 per cent of babies are born with a structural abnormality of the heart. The commonest problems are septal defects (holes in the walls between the two sides of the heart). In an atrial septal defect, the hole or holes are in the barrier between the two collecting chambers, while in ventricular septal defects they are in the barrier between the pumping chambers. The holes allow blood to pass from the left of the heart where the pressure is higher, to the right side. Babies are not blue, but this puts extra blood flow through their lungs and makes the heart work harder and children need to be seen by a cardiologist. Some small holes close up naturally but if they do not, or they are very big, children need surgery. Another problem is a narrowing (coarctation) of the aorta shortly after it's come out of the heart (above, right) which reduces the blood flow to the rest of the body; this too needs surgical treatment. Other rarer and more serious heart abnormalities have been found, so children with 2q37- are recommended to have an echocardiogram and cardiac assessment at diagnosis.



Kidney abnormalities are said to affect 10–11 per cent. Some children have a small kidney on one side that doesn't function well. This can cause progressive damage and high blood pressure so the child needs monitoring. Horseshoe kidneys (the kidneys are joined by a bridge of tissue) are quite common; or one kidney can be on the wrong side and joined to the other kidney. So-called 'duplex' kidneys with two sets of ureters (tubes leading to the bladder) can occur, causing backflow of urine up the ureters and kidney infection. An ultrasound scan should identify any of these kidney anomalies and if found the child should be seen by a kidney specialist. Children with 2q37- may also be more likely to develop kidney cysts, so the kidneys should be screened periodically.

Recommendations for kidney screening include ultrasound at diagnosis; further testing if they are having urinary tract infections; ultrasound

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for cysts at four and 15 years; Wilms' tumour screening (see *Question Time*) if 2q37.1 is involved.

Gastrointestinal problems can include blockages at any point in the gastrointestinal tract. A gastrointestinal blockage is a surgical emergency. Additionally, pyloric stenosis has been seen, where the ring of muscle at the outlet of the stomach becomes thickened and narrowed, stopping food leaving the stomach and causing forceful vomiting at a few weeks of age.

The intestine can also twist on itself. It should be anchored at various points but if the small intestine and part of the large intestine isn't anchored properly (malrotation), it can twist (volvulus). This is either a surgical emergency or may present later with episodes of vomiting, disproportionate abdominal pain or even red stools. Doctors need to be aware of this possibility if a child has these symptoms.

Where lungs and breathing are concerned, children with a deletion including 2q37.1 are the most at risk of problems. The commonest is 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.

Diaphragmatic hernia has been seen, usually picked up on the 20-week pregnancy scan and dealt with soon after birth. Rarer problems include choanal atresia, where the back of the nose is blocked, so the baby has problems feeding from birth.

Structural brain abnormalities seem to be more common in those with bigger deletions, affecting 6–8 per cent. Possible problems include hydrocephalus, where the fluid-filled parts of the brain are enlarged and pressure within the brain may be increased; holoprosencephaly where the two halves of the forebrain haven't separated properly; and problems with the cerebellum that mainly controls balance and coordination. A child who has suggestive findings should have a brain scan.

Up to six per cent of children have a genital anomaly. Undescended testes, a common problem regardless of chromosomes, may need to be brought down surgically; the testes may be small and poorly functioning; hypospadias, where the outlet of the tube from the bladder (urethra) is on the underside of the penis, may need surgical correction if it's significant; in a girl the uterus may be divided by a septum (division) in the midline.

As children get older, watch for lax joints and loose skin that scars easily. Children may have flat feet and need adapted footwear and physiotherapy. Congenital hip dislocation is a bit more common in 2q37-; this is screened for at birth but if the newborn screening was normal and concerns remain, a specialist orthopaedic assessment may be needed.

Spinal curvature may be more common than in typically developing children, due more to low muscle tone and muscle imbalance than to vertebral abnormalities. It may need monitoring, bracing or surgery.

In terms of growth, short stature has been found in 23 per cent and this may be an underestimate. The short stature is relatively mild, body proportions are normal and there is no obvious hormone deficiency. Obesity tends to increase with age although the cause is unclear.

Facially, children with 2q37- have a resemblance. Typically, they have thin, neat arched eyebrows with a flare towards the nose, eyes that are typically deep set, the tip of the nose hangs down a little, the nostrils may look flared or underdeveloped, the upper lip is rather thin, and the V in the middle is not strongly developed. The ear shape may be slightly unusual, the palate is commonly high-arched and hair on the scalp may be sparse.

In around half the children, the bones in the palms of the hands (metacarpals) are shortened as are the bones of the fingers (phalanges) known as brachydactyly. The feet are also affected, so the toes are set back and the feet are often short and broad which can make finding shoes difficult. This is not usually obvious in a baby, but becomes more evident with age.

From what is known about development and learning, learning disabilities are variable but usually mild or moderate. It is reported that one adult is a librarian's assistant, another with intelligence within the normal range is a college student but has behavioural features on the autistic spectrum. In Dr Wilson's experience, most adults are not able to live independently.

Structural eye problems are rare but short and long sight, astigmatism and squints are more common in chromosome disorders and are worth screening for. Neonatal screening should pick up hearing loss; glue ear is frequent in 2q37- and should be checked for.

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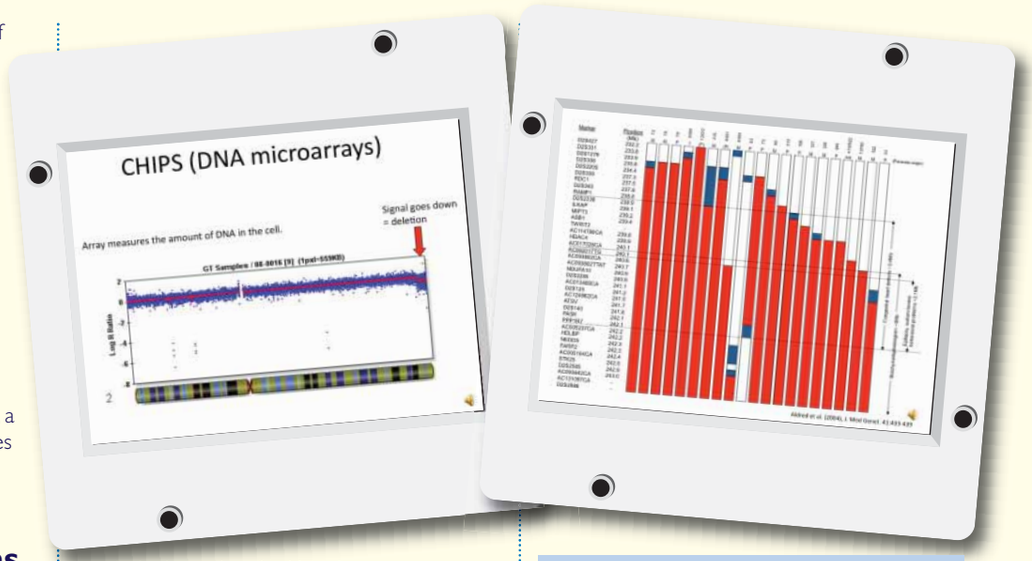
Reports suggest that around 30 per cent of children with 2q37 deletions have an autistic spectrum disorder. There are also reports of hyperactivity with attention deficit, intermittent aggression, obsessive compulsive disorders and sleep disorders.

Seizures have been reported in around 30 per cent. They are of various types but they usually respond to standard treatments. Most children with fits don't have any structural brain abnormality.

As for the long term outlook, the impression is that smaller deletions are linked with a milder condition but the correlation isn't precise. Generally speaking, a lack of malformations and of autistic features suggests a better outlook.



Progress in molecular studies of 2q37 deletions

Dr Micheala Aldred, assistant professor at the Cleveland Clinic, Ohio and Case Western Reserve University, has studied 2q37 deletions in a series of 20 individuals.

Dr Aldred's team has applied microarrays and FISH (adding a fluorescent dye to a DNA probe that seeks out the piece of DNA on the chromosome that it matches) to see which genes are deleted and whether they match the clinical features. They have also tried to map the deletion size: can they look at the extent of the deletion and predict how children will be affected?

Using new diagnostic techniques, the break points at 2q37 can be identified much more precisely than when looking down a microscope using conventional chromosome analysis. In most people there is just one break and the end of the chromosome gets lost, known as a terminal deletion. Microarrays have improved diagnosis so in one case what was thought to be a terminal deletion was in fact interstitial, with two breaks, preserving the end of the chromosome.

Dr Aldred's team has focused on common issues such as facial appearance and developmental delay. They looked at the shortened bones in the feet and hands (metatarsals and metacarpals) and 'characteristic behavioural problems': features of autistic spectrum disorder, including aggression and self harm. They looked at epilepsy and congenital heart defects, which affected one child in five in their series. They didn't look at kidney problems or brain abnormalities because there weren't enough in the series.

They found that in some cases children with quite similar-sized deletions had a lot of variability in their clinical picture. Looking at the size of the deletion, it wasn't very easy to say for sure how significant the clinical problems would be. But they identified a 3.4 megabase (3.4 million base pairs) section that was associated with heart defects, a slightly smaller 3 megabase (3 million base pairs) section extending to the tip of the chromosome associated with the shortened fingers and toes and a smaller 2.1 megabase region where they cautiously felt that a gene/s might be responsible for the epilepsy and behavioural problems.

> *"I would agree that some of those abnormalities (kidneys, brain) probably correlate with the larger deletions but if they were not common in our group we couldn't find a correlation."*

The team also found that it made no difference if the deletion came on the chromosome 2 from the mother or from the father.

In summary, there was a lot of clinical variability and a larger deletion did not necessarily mean it was clinically more severe.

> *"We can't easily predict the clinical outcome from the size or position of the deletion but we will probably find in future that the very small deletions at the very tip may have a less severe phenotype."*

Hot off the press is the news that losing a single gene can probably account for the shortened fingers and toes, possibly the heart defects and perhaps even the developmental delay. Collaborators at Virginia Commonwealth University have identified a single responsible gene. The behavioural aspects, however, probably can't be pinned down to an individual gene. Autism in particular is complicated, and

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many genes as well as environmental effects are involved.

Wilms' tumour

Dr Aldred clarified what is known about 2q37 deletions and Wilms' tumour. Of more than 100 cases of 2q37 deletions published in the scientific literature, three children have developed Wilms' tumour at a very early age. Two of the children had large deletions including 2q37.1 and the other child had an extra risk factor for Wilms' tumour. This shows that Wilms' tumour is overall very rare among those with a 2q37 deletion. Among children with Wilms' tumour but without a 2q37 deletion, cells taken from the tumour showed a deletion from the region at the top of 2q37.1 on the boundary with 2q36.3. Over 200 tumours were studied and this abnormality was present in 4–10 per cent.

> *"There are so few cases that we don't really know what the risks are but all the available evidence points towards probably larger deletions possibly having a slightly higher risk."*

Practical Strategies for Developing Communication Skills

Nicola Lathey, a specialist speech and language therapist in special needs, reviewed the types of communication problems that a child with 2q37- might have and how parents and professionals can help.

Speech is how words are articulated; language is about putting words together into a sentence and communication is the overall picture of how successfully someone can project themselves and interact with different people, socially and with speech. Being a good communicator doesn't need speech.

2q37- affects children in an extremely wide range of different ways but problems might include a short attention span, some characteristics of autism, slightly unusual social skills such as staying on one topic for a long time.

A parents' survey showed a huge range in when a child might acquire their first words from around 18 months (in line with normal development) to about 6.5 years. Some children didn't achieve verbal language and use an augmentative or alternative system such as picture exchanges or a computer. There was also a significant delay in being able to put words into sentences.

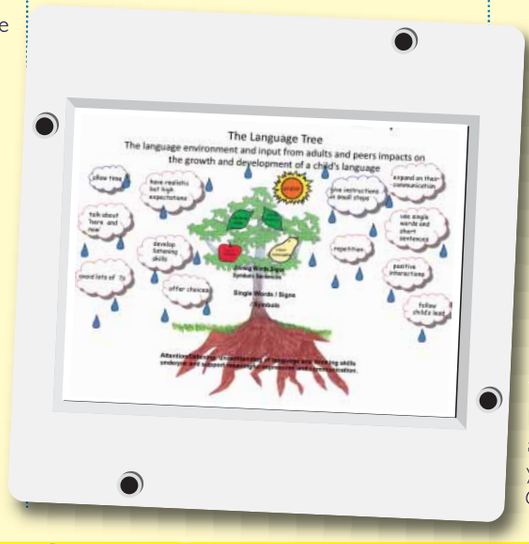
A delay in speech sound development was also noted from the parents' survey and there could be many reasons to explain this. One of the most likely is the high prevalence of hypotonia (low muscle tone) in children with 2q37, which affects articulation; with muscle weakness difficulties will affect intelligibility. Some nerves leading to the muscles in the face and articulators have a sensory and a motor component. Exercises like blowing bubbles or sucking straws often target only the motor component, neglecting the sensory side. Approaches like facial massage, tapping and brushing can be helpful to stimulate the sensory component. An S&LT should be able to provide a programme for oro-motor development.

How can one help children with their speech, language and communication? With children who struggle to learn that a word represents an object one might use a signing system, such as Makaton, revived on television in the UK by the BBC's CBeebies' Mr Tumble. All the research shows that far from stopping a child from talking, signing helps later language development. Some children can use symbols, pictures or photographs, possibly in a picture exchange system [PECS].

Joining single words can be a difficult step; a child needs to learn about 50 words before they start joining, but once two-word phrases take off, joining words into short sentences usually expands. A S&LT might start with phrases like *More ball* or *More book*; or *Bye-bye mummy*. As the child gets better at joining, try noun-verb combinations like *Mummy jumping* or *Dog sitting*.

Any hearing difficulty should be ruled out but there may be a problem staying focused. Parents can help by developing their child's listening skills, such as listening for animal noises or noises in the environment and playing sound-based games. Parent-child interactions should be positive and fun; a parent who is worried about their child's language can unknowingly apply pressure, eg *'say hello to daddy'* making some children avoidant. Allow processing time – try counting silently to 10. Use language appropriate to the child's level – single words or two-word phrases. Repeat and repeat again: a typically developing child needs to hear a word and see the object at the same time more than 500 times before attempting to say that word. A child with a language problem needs perhaps two or three times as many repetitions. Follow the child's lead and interests. Offer them choices. Avoid question overload since a child with a language problem won't answer. Instead, just say the answer ie instead of saying *What's this?* Just say *"bottle"*. Expand on the child's own communication using the formula *Match plus One*. If the child says *I'm drinking water*, say *I'm drinking fizzy water*. Give instructions in small steps. Talk about the here and now. But for a child with good language, review the day at bedtime, sequencing it to expand their language. Even those with good communication can find it hard to structure and sequence their thoughts into first, next and last.

Have realistic but high expectations and try and stay one step ahead of your child. When you praise your child, be specific: *Good talking! Good listening!*



Challenging Behaviour in Children with Special Needs

Emma Hyde, Clinical Nurse Specialist (Learning disabilities and mental health) with the Oxfordshire Learning Disability Child and Adolescent Team, gave parents more tools for dealing with challenging behaviour.

Difficult, problematic or challenging behaviour has a broad definition: 'culturally abnormal behaviour/s of such intensity, frequency or duration that the physical safety of the person or others is likely to be placed in serious jeopardy, or behaviour which is likely to seriously limit use of, or result in the person being denied access to, ordinary community facilities'. The most important aspect is denying access to ordinary community facilities.

Ask yourself: *When does the behaviour happen? When doesn't it happen? How long does it last? Who is affected? What happens as a result? What doesn't happen?*

Using functional analysis, we look at what the person is getting out of the behaviour and try to substitute a more acceptable way of achieving the same outcome.

Record what happens, using an ABC chart.
A = triggers
B = behaviour
C = consequences, even unwitting ones

A home school diary can be used instead.

The aim of most behaviours is to gain something, initiate social contact, relieve anxiety or tension, reduce stress, get sensory stimulation, express emotion or avoid something. Seeking attention is not in this list, and it may be unwise to ignore a child with limited communication.

Phases of explosion

An explosion of bad behaviour follows a course that can last 10 minutes or four hours: trigger, escalation, explosion, de-escalation, dip.

What is the trigger? Sometimes you can't discover because inner thoughts, feelings, anxieties and stresses play a role. You may not realise that you are in the early stages of an explosion because the signs can be subtle. But if you can identify the trigger, separate the child from it.

During escalation, adrenaline surges through the system. Try to respond quietly, even faking calmness. Even being 10 per cent calmer helps. Remind the child of the rules and rewards for good behaviour. Model being calmer for them in your own behaviour.

If the trigger was a request, restate it, but avoid locking horns by making it easier for them to comply and above all avoid making new demands. Keep the background environment calm.

Once an explosion is reached, the priority is to be safe. Adrenaline powers up big muscles in the arms, legs and lungs ready for running away. It doesn't power up things like logical processing, negotiation or vocabulary skills and blood is taken away from those parts of the brain. Clear the environment. Then either get help or decide in advance what help you need.

After the explosion, adrenaline levels slowly return to normal over upwards of 90 minutes. Getting back to normal is very important for onlookers, such as siblings. Talking the outburst through can help but not while you are still feeling vulnerable.

A dip follows the de-escalation where noradrenaline takes over from adrenaline, bringing about lethargy, tiredness, confusion and guilt. Recognise the dip for what it is and wait until it has passed before planning long term strategies.

Longer term strategies to reduce challenging behaviour

Praising the desired behaviour is a well-known strategy but reinforcement must be immediate, contingent and consistent. It should be individualised and can lose effectiveness if used too much. Ignoring undesired behaviour by refusing to talk, avoiding eye contact, turning away or attending to someone else in an obvious way are other means of reinforcement.

Be aware that the behaviour may well get worse at first in what is known as an 'extinction burst'; so hold on.

Reward with a token system such as a star chart or find something really important to the child that can only happen with a particular behaviour. Many people give up after a week or two because the reward isn't enough or they get bored. Up the challenge, either using smaller rewards or demanding more for the same rewards. After 4–6 weeks the new behaviour should be a habit.

Modelling matters: are others at home doing what you expect your child to do?

Chaining is a way of making achievement and praise possible. Break a complex sequence like tooth brushing into perhaps 12 segments. In backwards chaining you do the first 11 jobs and the child does the twelfth. Once they've achieved that, they do the last two but they always finish the task off.

If you decide to begin a behaviour plan, agree on a system that works in all your child's everyday settings such as home, school and respite. Explain the plan to everyone involved in your child's care and tell them how you need their help. Set realistic time schedules and agree to evaluate how things are going.

Books

- *It can get better*
  by Paul Dickinson and Liz Hannah
- *Challenging Behaviour and Autism: Making Sense – Making Progress*
  by Philip Whitaker

Published by National Autistic Society

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Question Time

LW = *Dr Louise Wilson*
MA = *Dr Micheala Aldred*
ES = *Dr Eugen Strehle*
EH = *Emma Hyde*

Q ***How much more information would a microarray test give today compared with a FISH test four years ago?***

MA *At the moment a microarray test wouldn't give much more helpful information but in the future there might be a reason for going back.*

Q ***Is there a link between the deletion (2q37.3) and growth? If so, is it possible to predict the effects or severity?***

LW *There probably is a link. Adult stature below the normal range seems to be more common. There is a bell-shaped distribution of height in the general population. In people with 2q37, you get a similar distribution but it's shifted down a little, so some people are below what's considered to be the normal range, others fall within the normal range and fewer would come at the top end of the normal range. But in the published literature we don't have final height data of adults yet.*

Q ***Do children stop growing early or have a different growth pattern to normal?***

LW *There are no longitudinal data but the literature suggests that children don't have such a big growth spurt during puberty and stop growing earlier so may be shorter as adults than expected from their earlier childhood growth.*

Q ***Is there a link to iron or other deficiencies?***
Two children at the meeting have an iron deficiency, one stabilised with supplements, the other lost a lot of hair. One child has a high alkaline phosphatase level but low vitamin D.

ES *Iron deficiency is common in children and is usually diet rather than 2q37 related. Vitamin D deficiency can be related to diet or to exposure to sunlight; a high alkaline phosphatase level can be the first sign. Vitamin D deficiency can lead to softening of the bones; you need to replace the vitamin D.*

Q ***What is the incidence of epilepsy and how is it managed? What are different families' experiences? How many have uncontrolled epilepsy? How many have apnoeas? Are there any new advances in epilepsy treatment or cures? Are tics an unusual behaviour or part of the epilepsy?***

ES *Not just in 2q37- but in other chromosomal syndromes it's more common to have abnormal electrical activity in the brain and seizures or fits. Children with suggestive signs will have an EEG, perhaps a brain scan. Medications include sodium valproate, carbamazepine and lamotrigine.*

Q ***Our son has had every drug mentioned and still has uncontrolled epilepsy.***

ES *Sometimes children have epilepsy that is difficult to treat; they can try different combinations, the ketogenic diet or very rarely surgery.*

Q ***Are febrile convulsions more common? My daughter still has them at the age of 10.***

ES *They are common in all children from 6 months to 6 years and normally there's no need for anti-epileptic medication. There are also febrile convulsion syndromes with a genetic basis, so it might be worth going back to the neurologist to ask if they have considered that.*

Q ***Have any children outgrown their epilepsy?***

LW *It can happen.*

Parent *My son had absences at pre-school, an EEG showed nothing, and as he grew older he outgrew it.*

Parent *My 2.5 year old son had absences and 3 or 4 EEGs showed nothing but sleep apnoeas and a sleep study showed nothing. An MRI brain scan showed enlarged ventricles and fluid on the brain. Should we be looking to give treatment to control it? We are concerned that it could develop into something later on.*

ES *Absence epilepsy is a special form of epilepsy. If it doesn't show up on a simple brainwave test do a sleep-deprived brainwave test, although this is difficult in younger child.*

Q ***Do we need to worry about soft stools?***

ES *Acute diarrhoea that has lasted less than two weeks is usually viral or bacterial. If it's lasted longer than two weeks it could be 'toddler diarrhoea', where no treatment is needed. In older children, irritable bowel syndrome is a possibility but blood tests should also be performed to rule out coeliac disease and inflammatory bowel disease. Ask your GP for a referral to a specialist.*

Q ***Does development slow down or stop at a specific age? Is there any evidence of deterioration?***

LW *Not so far as we know.*

Q ***My child is pretty healthy now but are there any illnesses to watch out for?***

LW *There is a suggestion that children may be more likely to develop kidney cysts as they get older, based on two children in the medical literature who had normal kidney scans in the first two years of life but were found to have kidney cysts later. Kidney cysts are quite common in adults and most do not need treatment or cause problems. They are not cancerous. Occasionally the cysts can cause pain or be associated with blood or infection in the urine for which more detailed investigations may be necessary. Because of this, it is currently recommended children have kidney ultrasound scans at diagnosis, at 4 years and at around 15 years.*

There have been three reports of children with Wilms' tumour who all had breakpoints at 2q37.1. Wilms' tumour is a form of kidney cancer which affects children, mostly under five years. Most Wilms' tumours respond well to treatment and most children can be cured. In children considered to be at greater than five per cent risk of Wilms' tumour, screening is available by ultrasound scan or a combination of ultrasound scans and abdominal palpation. It is not clear what the absolute risk for Wilms' tumour is in children with 2q37 deletions and whether it exceeds five per cent but the most recent reviews recommend screening for children with breakpoints involving 2q37.1 or deletions encompassing 2q37.1.

Excessive weight gain in later childhood and adulthood seems to be common in people with 2q37 deletions and it is

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recommended that parents watch out for it and try to prevent it.

Some families with children aged 8 or under reported that their children ate a large amount but had difficulty putting on weight. Other families reported overweight. A father commented that his daughter started putting on weight when she was around 8. They try to ensure that she eats healthily and takes exercise, but her hypotonia is a barrier.

Q ***Are children prone to Graves' disease or other thyroid problems?***

LW *Not so far as we know.*

Q ***Do families have experience with dislocating joints?***

2/17 families reported dislocating joints; one reported hyperflexible joints.

LW *Loose joints have been reported quite frequently in children with 2q37 deletions and low muscle tone is also common. Both will make children more susceptible to dislocations. Congenital hip dislocation has been reported in a small number of children.*

Q ***Is there any evidence of deterioration at an early age?***

LW *Not so far as we know.*

Q ***Do people with 2q37 deletions have fertility problems?***

LW *Anyone with a 2q37 deletion who has children will have a 1 in 2 (50 per cent) chance in each pregnancy of passing the condition on. To date there has been one anecdotal report of a woman with a 2q37 deletion having a child, and the child was also affected. There have been no reports of men with 2q37 fathering a child.*

For females, there have been reports of abnormal womb shape (bifid uterus) and abnormalities of the ovaries (dysgenetic) which might be expected to reduce fertility. However, girls with 2q37 deletions generally seem to go into puberty and have periods normally which suggests they are likely to be fertile. Certainly, if they may be sexually active and they and their carers wish to avoid pregnancy, contraceptive measures need to be taken.

For males, there have been several reports of physical differences such as hypospadias, undescended testes, and small or abnormal (dysgenetic) testes which might be expected to reduce fertility. However, there have been no detailed studies of fertility in males with 2q37 deletions.

Q ***Are there any more surprises – life threatening issues or life limiting conditions that might develop?***

LW *There is nothing particularly life-limiting unless you have an important problem like a heart malformation. Epilepsy can also have an impact.*

Q ***How old is the oldest known person with 2q37?***

A *There is a report in the literature of someone in their 60s and a case report of a brother and sister in their 50s. The oldest person on the Unique database is 42. Almost certainly there are more adults than we know about.*

Q ***Are there any big changes around puberty? Has early onset puberty occurred?***

LW *The literature suggests that girls with 2q37 deletions start their periods at a similar age to unaffected girls.*

A few families suggested that their child experienced either early puberty or early adrenarche (the early appearance of pubic and armpit hair and body odour without other signs of puberty).

Q ***Compulsive behaviour: my son's behaviour is generally good but if for example his iPod runs out of battery it can just suddenly get thrown. Afterwards he is unaware of having thrown it and bewildered as to what happened.***

EH *It's common in the explosion phase not to have a logical explanation of what's happened. You can work on social stories, telling other ways to respond if the iPod runs out.*

Q ***He attends a mainstream school with an autism unit. Some children function less well than him and he copies their behaviour, saying things like My iPod is poopoo.***

EH *A child is seeking a reaction when he says this word. So suggest another word – any word he's never heard of – is even naughtier than poopoo.*

In a show of hands, families reported the frequency of certain problems. 17 families were present

	YES	NO
Showing body parts	12	2
Excessive obsessions	10	4
Making up stories	3	6
Self harming	10	7
Dental issues	8	

This report covers the specific 2q37 presentations as well as those on speech and language and behaviour and the main questions asked by families. The slides from the presentations are available on the members-only part of the *Unique* website, as well as the slides on *The Child with a Chromosomal Disorder from a Paediatric Perspective* [paediatrician Dr Eugen Strehle]; *Creating a 3D model of typical faces in 2q37-* [Peter Hammond, Professor of Computational Biology, Institute of Child Health, London]; *Sleep issues and how to tackle them* [Pattie Everitt, Sleep Counsellor] and *What is 'normal' development?* [Karen Sutherland, clinical psychologist in training].

Dr Eugen Strehle

Professor Peter Hammond

Pattie Everitt

Karen Sutherland