

Koolen-de Vries Syndrome Study Weekend



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In late 2015, Unique member Mandy Hazelgrave approached us about the possibility of running a study weekend for families with children and adults who, like her daughter Leanne, have Koolen-de Vries Syndrome (KDVS). We were keen to help and said that we would try to raise some of the funds needed but the families themselves would also have to fundraise if the weekend were to go ahead. Over the following months, they showed amazing commitment, raising almost £2,000 and we at Unique were pleased to be able to secure a grant of £5,800 from Awards for All, part of the Big Lottery Fund.

Over the weekend of 30th September – 2nd October, 28 families, plus Beverly and Craig from Unique came together in Leeds, England. We were delighted and very honoured to be joined by Dr David Koolen (after whom the syndrome is named, along with fellow geneticist Dr Bert de Vries) and his PhD student colleague, Katrin Linda, who both came in from the Netherlands. Having had a relaxed Friday evening which was a great chance to get to know friends old and new, the study weekend got into full swing on Saturday morning. The 'Kool Club' opened at 9, with childcare and lots of activities for the children and affected adults alike, including face painting, a chill out space and a dance workshop. This meant that parents were able to relax and listen to the presentations safe in the knowledge that their young people were being well cared for.

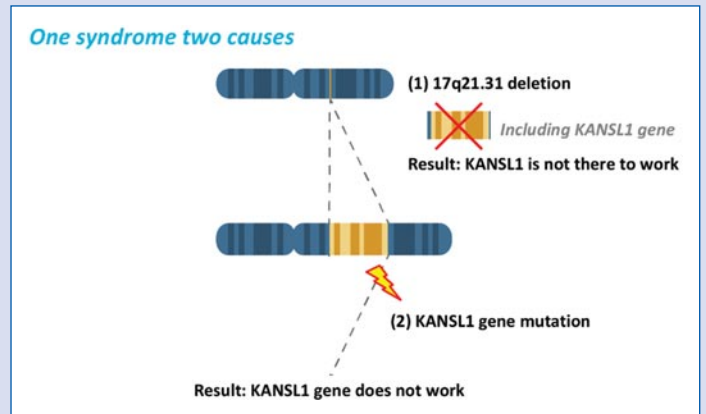
The morning session was taken up with presentations from Dr Koolen and Katrin Linda.

What causes Koolen-de Vries Syndrome and how was it discovered?

Dr Koolen began with an overview of KDVS, explaining that it has two possible causes: a 'deletion' on chromosome 17 (a '17q 21.31 deletion'), involving around 500,000 – 600,000 base pairs

of DNA leading to loss of the KANSL1 gene, or a genetic mutation within this gene. Dr Koolen used a car metaphor, either the car is not there at all (deletion), or there is a problem, such as a wheel missing (mutation); either way the result is the same – KDVS.

Dr Koolen reported that in 2006, over 50% of children with an intellectual disability had no formal diagnosis. The introduction of a new type of genetic test, called microarray or array-CGH analysis, meant that it became possible for much smaller changes in a person's chromosomes to be identified than had previously been possible. Such a test was done on a young lady called 'Anna' in the Netherlands and showed that she had a 17q21.31 microdeletion. Further tests were carried out on others and 2 or 3 other children were identified with the same microdeletion and accompanying symptoms, moderate learning disabilities, severe hypotonia, severe motor delay and similar facial characteristics. A new syndrome had been discovered and initially named 17q21.31 microdeletion syndrome, later becoming Koolen-de Vries Syndrome, after Drs Koolen and de Vries. Three separate groups of genetics researchers (Koolen and de Vries in the Netherlands, Shaw-Smith and Carter in the UK and Sharp and Eichler in the USA)



Graphic from Dr Koolen's presentation showing the two causes of KDVS.

published separate papers back to back in the same medical journal, reporting this recurring genetic disorder.

Some genetic syndromes, for example Angelman Syndrome and Prader-Willi Syndrome were first recognised due to similar physical characteristics among those affected, eg facial features. However, KDVS was recognised by its genetic basis first, and then by the physical characterisation (a 'genome-first characterisation' as Dr Koolen put it). There are now in excess of 500 known cases of Koolen-de Vries Syndrome in the UK, Europe, the USA and Australia, with an estimated frequency of 1 in 16,000 newborn babies and Dr Koolen went on to say that it is estimated that 1 in 2,000 children with global developmental delay have KDVS, most due to the deletion in 17q21.31. Ten-20 children with KDVS are known to have the KANSL1 mutation.

KDVS is a multi-system disorder, with possible symptoms including hearing, vision, neurological and skin conditions, although not all are present in all children. Children have a wide range of abilities, although the size of the deletion is almost identical between children and Dr Koolen feels that the degree of

severity of their symptoms is likely to be due to other genetic factors, something we also see in other syndromes. He said that it is difficult to pinpoint those other factors, which as well as genetic could also for example include environmental or neonatal factors.

"We need the numbers!"

Dr. Koolen reported on collaborations he had been involved in with groups in Australia and the GenIDA International project (a database which includes 113 active participants with KDVS). He said that gaining as much clinical data as possible is key ("we need the numbers!") as it helps to predict health outcomes for the child and helps to answer the questions parents have, such as 'what are the chances of my child developing epilepsy?' Dr Koolen encourages families to invest the time to take the GenIDA survey (<https://genida.unistra.fr>) and said there is a link on the Koolen-de Vries Syndrome website. Some of the parents at the event who had already done so urged others to take the survey as well.

Question Time

Parents had submitted questions in advance and Dr Koolen ran through them.



Dr Koolen presenting.

Communication seems to be a prime concern, with parents frequently asking: 'does speech always arrive?' He reported that 10%–11%, or 4 of 35 children he had studied (his 'in-house data'), had remained non-verbal, although cautioned that this was a snapshot and that some children speak by the age of 5 years, some later on. Typically, first words are delayed but usually come between the ages of 18 months to 3 years or later. All those studied have expressive speech delay. Those with KDVS have a mixture of apraxia and dysarthria, though once language develops some children are able to catch up quite well.

Data from GenIDA shows that around 30% do not speak, although this is likely to reflect that most of the data is about young children and with age and increasing number do begin to speak. In adulthood, around 70% are able to read. One Mum reported that her son can express many more words than he understands, being non-verbal but using AAC (Augmentative and Alternative Communication) methods.

Behaviour was the next question Dr Koolen addressed. In 45 children studied in a non-longitudinal analysis 57% had behavioural/ neuropsychiatric problems. Issues included Autism and ADHD. Looking at the data in GenIDA, 70% have behavioural problems, with examples including repetitive behaviours, obsession, anxiety, phobias, hyperactivity and attention deficit.

Epilepsy is another concern

and Dr Koolen referenced a study undertaken by Ken Myers in Australia. Seizures were seen in approximately 50% of those studied (31 people aged 2 to 35 years), with a median onset of 3.5 years of age. The majority had refractory epilepsy which can be tricky to treat, with focal seizures the most frequent. There are usually prominent autonomic features. In 21 patients, the seizures were prolonged and hard to treat and 13/31 of those studied had structural anomalies of the brain including absence of the corpus callosum (ACC) and defects of the hippocampus.

Visual Impairments such as strabismus (present in 41% of those studied) and hypermetropia (in 38%), as well as myopia and nystagmus, are also relatively common, as is cerebral visual impairment in which the brain doesn't process the stimulus.

Another issue Dr Koolen felt parents should be aware of is **Melanoma**. He said that 18% of children studied were found to have more than 50 moles on their skin. This suggests a potentially increased risk of developing melanoma. He cautioned that most moles never cause a problem but that someone with a high number is at greater risk and should be monitored on an ongoing basis. Other ectodermal problems also feature in 60% of people with KDVS, for example brittle nails, skin pigmentation and hair and teeth issues.

Parents had also asked questions about their child's **weight**. Most children seem to be slightly shorter than the average for their age and of a

lower weight, although usually still within the normal, expected range. Some children are very small and have growth hormone deficiency but in general Dr Koolen did not feel weight is a significant problem.

Musculoskeletal problems

such as hyperlaxity, scoliosis, flat feet, and hip dysplasia do feature though and more than 40% of children have some degree of joint laxity. Other, less frequent issues include the child having an abnormally-shaped skull (such as dolicocephaly, trigonocephaly, brachycephaly or scaphocephaly) a metopic ridge, bitemporal narrowing, gut issues and tooth grinding.

The final question was about whether KDVS can currently be recognised during pregnancy. Dr Koolen explained that yes, it is possible to carry out a test in an amniocentesis sample that will detect the 17q21.31 deletion. He said that having had a child with KDVS, the chance of future siblings also being affected is very low, at less than 1%; so the risks to the pregnancy of having an amniocentesis need to be weighed up very carefully. Cases known to date are 'de novo' (not inherited from either parent) and pre-natal testing can be done but you should discuss and carefully consider the risks associated with this.

Dr Koolen was also asked about any direct link between parents having an inversion in 17q21.31 and their children having a deletion or duplication of this segment of chromosome. He replied that 40% of the general population carry an inversion in 17q21.31 but only a tiny percentage of the population have KDVS. Therefore he said if you do not carry the inversion then it is not possible to have a child with KDVS but if you do carry the inversion you still have only an extremely low chance of having a child with KDVS.

Dr Koolen concluded by saying that KDVS is not caused by the parents, it is not due to something you did during pregnancy or a particular behaviour, it is just something that happens in nature.

KANSL1 and Koolen-de Vries Syndrome

After a break for coffee and a chance to chat to other parents, Katrin Linda, a PhD student working with Dr Koolen in Nijmegen, Holland, took over to talk about the KANSL1 gene and why it is important to know more about its function. She picked up on what Dr Koolen had said earlier on, that KANSL1 haploinsufficiency (lacking one copy of the gene) causes KDVS. Knowing and understanding the role this gene plays could help to treat specific symptoms and enable development of more specific and more effective drugs.

KANSL1 is part of the 'non-specific lethal complex' (NSL). It is needed as part of the mechanism to open up the protein (histone)-DNA complex in tightly coiled chromosomes. By doing this the genes on the DNA, become more accessible in the first stage of gene expression (DNA transcription). Loss of a copy of the KANSL1 gene means this "opening up" process does not work as well and the DNA and genes are less open to being expressed.

Using Animals and Isolated Cells to Model KDVS

Katrin then went on to describe some very complicated research techniques and first talked about the use of specific animals to model KDVS, beginning with the fruit fly, which has a gene called Wah, which is similar to KANSL1. Studies by Lone et al, 2010 and Koolen et al 2012, had

shown that if you knock out this gene the fruit fly's capacity to learn is reduced. There is a 25% reduction in learning ability. Further tests were carried out on mice and in an object recognition task, those mice with the deletion were found to have an impaired short-term memory compare to those without the deletion who were able to return to and recognise objects they had already seen. Katrin said that the advantages of using mouse models are that mice and humans share 99% of their genes and symptoms/behaviour can often be mimicked by mutating the corresponding mouse gene. Drugs can then be tested in the mice and their effectiveness measured. However, she cautioned that the mouse brain is different to the human brain and that symptoms and behaviour are not always 100% mimicked. Drugs that proved to be effective in mice were not always as effective in humans and vice versa.

In 2006, Professor Yamanaka and colleagues in Japan developed 'induced pluripotent stem cells' (iPS cells) from adult human cells, eg skin cells, which can then be 'changed' into any type of body cell. This enables research to be undertaken on isolated human cells of choice that would not otherwise be possible in the whole human body and that avoids the use of animals in research. For instance iPS cells from healthy people and from people with KDVS can be turned into brain cells (neurons) to provide a model test system of normal control cells and KDVS brain cells on which different drug therapies can be tested. Indeed, a recent KDVS patient day in America involved cells being collected from parents and their affected children as another way of furthering this type of research into the syndrome.

Immunocytochemistry can be used to look at different building blocks of the cell (different structural proteins). Using such immunocytochemical models, eg the degree of opening of the NSL complex can be assessed and then different test conditions can be imposed to try to reverse the effect of the KANSL1 gene. Katrin explained that it is even possible to use microelectrode arrays (MEAs) which are little electrodes in the culture dish which can record the electrical activity of isolated neurons. These measurements can be done at different time points during neuronal cell development, making it possible to screen different drugs in the culture dish to observe their effects. Using this method it could be seen that in normal healthy cells neuronal communication was fine but in KDVS neurons communication was disorganised. When looking at normal cells versus those with the KANSL1 mutation, it is possible to observe at what point in the cell's development things go wrong.

Katrin concluded her presentation by answering a question raised about gene editing techniques such as CRISPR/Cas9. In mammalian cells these techniques can be used to target specific DNA regions of interest. When DNA is cut, there are mechanisms to repair it and it may be possible to correct a genetic mutation, for example using DNA which does not contain the mutation. This is a potential way that single gene disorders could be treated in the future, although Katrin emphasised that this remains a long way off and that a large deletion such as that seen in KDVS involves loss of not just one gene but of a large segment of genetic material involving six genes, including the critical KANSL1 gene. It was also emphasised that although KDVS patients have the same genetic loss, their

symptoms are not always the same. CRISPR/Cas9 does though enable researchers to examine the effects of a lack of the KANSL1 gene by creating a mutation in the single KANSL1 gene.

The Kool Club closed for lunch to give the staff a well-earned break and all the young people were excited to tell everyone what they had been doing during the morning session. There were lots of painted faces and even some painted arms on display (and clothing too, though we're not sure that was intentional)! With everyone refreshed, the young people went back to the Kool Club and parents returned for the afternoon workshop sessions.

Speech and Language Workshop

The first of the afternoon workshops was led by Nicki Arkell and Ben Bolton from Speech and Language and the Stammering Support Service at Leeds Community Healthcare NHS Trust.

Using research undertaken by Dr Koolen and others, it is known that with KDVS there is generally late development of first words and this usually happens between the ages of 18 months and 3 years, sometimes later. Children tend to follow a normal but delayed pattern of language development. There may be some discrepancy between comprehension and expressive language, with comprehension more advanced.

In terms of speech development in those with KDVS, it may be that low muscle tone has an impact. There are some motor planning and speech planning issues (dyspraxia) and some phonological difficulties, all of which affect the quality of speech.

Nicki and Ben used the 'speech pyramid' to illustrate the different stages involved in

learning to speak, including looking and listening, play, understanding, talking and pronunciation. With syndromes like KDVS, these do not always follow a normal path or pattern. The pyramid shows that adult – child interaction is also important in helping the child to learn.

Stammering

One of the topics submitted in advance that parents wanted to cover was stammering. In considering why a stammer might develop, Ben said that it is important to consider the **demands** made on the child. Talking on a 1:1 basis with someone you know for example, is usually low demand whereas presenting to a group of people in public is likely to be higher demand. Demands can include the vocabulary used, environmental factors (is it noisy for example?) and other, perhaps self-imposed demands. Then consider the child's **capacities**. How are they able to meet these demands? Do they have full mouth control or an awareness of rhythm? There may be particular challenges here for those with KDVS. Emotions such as anger, nerves, tiredness, level of confidence and a child's personality also come into play and can have an effect on speech and stammering. Bringing down such demands can help and listening skills can be key (you listening to the child and vice versa).

Strategies to help Communication

Ben and Nicki ran through some communication systems that parents might like to try or discuss with their speech and language therapist/child's school where applicable. Examples given included:

- Makaton, a language system using signs and symbols, (**see www.makaton.org**)
- PECS, the Picture Exchange Communication System
- Choice boards, enabling the



Ben Bolton and Nicki Arkell presenting.

child to make a definite choice about something they would like to eat, drink (eg a choice between water or juice), or play with, etc

- Communication books, often with symbols the child can point to, again to make choices or ask for things
- Spoken language – modified for the child

Ben and Nicki explained that many speech and language therapists would look to build in a little of everything, as appropriate to the individual child and their capacities. The aim is to help develop spoken language by helping the child to interact with us and to reduce the frustration the child feels around difficulty with communication.

Visuals can often be used to support this development of language. Begin with an object of reference (eg a cup), create a line drawing of it and maybe then used a photograph of it or symbols, then do the same for other objects. This can be developed into a visual timetable so that the child knows what's coming next and also to refer back to what has been completed. A simplified version of this is a 'First and Then' board which is often used in the early years and can be used to say to the child 'first school work, then drink' for example. Ben and Nicki said that some children have varying abilities, their language abilities may go beyond their comprehension or play skills for example so it is important to always try to match the visual to the child's level of understanding.

MacDonald's steps to communication

This is a way to help parents to think about their own communication and the need to go down to the child's level if we are to help them, then try to 'nudge up' a level as the child is ready. Tips include:

- keep language simple: use 1-2 word sentences
- reduce questions: questions are a way to teach and test but early on, just talk about what you can see and leave silences to give the child a chance to respond
- repeat key words only: this helps to show you have understood the child and reinforces this
- follow the child's lead
- sing favourite songs with them

Above all, accept all their attempts at communication
Some other specific

approaches to speech and language development were then discussed. **Intensive Interaction** involves putting yourself 'in a bubble' (not literally!) with the child for a specific period each day to stop everything else to focus solely on communicating with them. This can be as little as 10 minutes or much more, depending on the child. The **Hanen Program** is a Canadian approach which trains parents and the other important people in a child's life to give them the skills they need to help develop the child's language and communication skills. **Core Vocabulary Therapy** is often used with older children who have dyspraxic difficulty and the **Nuffield Approach** can be used by speech and language therapists to manage developmental verbal severe speech disorders. Nicki and

Ben also said that parents could use **listening and attention games** to build speech sounds, making it functional and fun, for example using animal noises or car noises and listening back to the child, showing attention. When out of the house, make an effort to point out sounds such as dogs barking, aeroplanes overhead. Take time to listen.

In summary, Ben and Nicki said that speech and language therapy can never take a 'one size fits all' approach. There are lots of different approaches as every child is different and brings their own needs and abilities. In answer to a question about difficulties with sound production, muscle tone, dyspraxia and speech planning can all be significant factors and research is being done into how oral cavities and having a high roof of the mouth affect speech development. Being tired and/or unwell is also likely to have an impact.

Ben and Nicki have kindly provided Unique with a copy of their presentation. Please contact us if you would like to see it and we will email it to you.

Sleep Workshop

The second of the afternoon

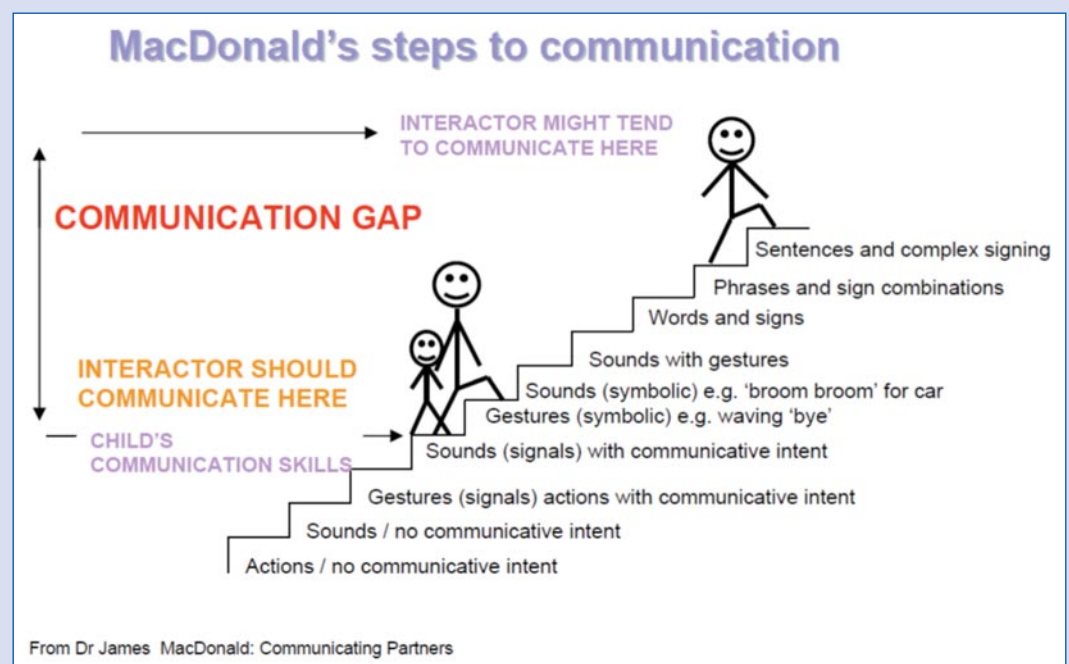


Figure 1 MacDonald's Steps to Communication.

workshops was led by Claire Varey, Sleep Practitioner at Cerebra who provide information and guidance to families. Problems with their children going to sleep, staying asleep and early rising had been identified by lots of parents in advance of the study weekend so it was a very relevant topic for many of the families, as for many families affected by other rare chromosome disorders.

Claire started by saying the need for sleep is still not fully understood but it helps biologically, with focus, concentration and memory and is important for emotional well-being. Children with additional needs have higher instances of sleep disorders than typically developing children.

The Sleep Cycle and Stages of Sleep

Circadian rhythms are biological cycles that repeat about every 24 hours. They include patterns of sleeping, waking, activity, rest and eating. The time at which a person falls asleep is linked to their body clock which is reset each day by the use of cues such as meal times, bed and waking time and differences in light which the eyes can detect (even when you're asleep). This all helps the body detect when to produce Melatonin, a hormone which induces sleep. Melatonin is suppressed by bright light, eg daylight but produced later when it gets dark.

Humans sleep in stages:

Non-Rapid Eye Movement (NREM): moves from light sleep from which a person can be easily awoken, into a slightly deeper sleep with slow rolling eye movements and occasional sleep jerks then into deep slow wave sleep, when blood pressure, heart rate and breathing slow down. This is when a person can be very difficult to wake and confused if woken.

Rapid Eye Movement (REM):

characterised by intense brain activity and dreaming, our eyelids usually flicker ('REM'). It occurs several times during the second half of the night's sleep, but comprises the smallest portion of our sleep cycle and involves an inability to use muscles, although we can use the diaphragm to breathe and eye muscles.

Parents of children with KDVS report that night waking or early waking (ie too early!) as significant issues. Claire explained that we all wake through the night but don't all have an ability to get back into the next sleep cycle. When we wake up and then go back to sleep, we don't go back into deep sleep but more into an REM pattern.

What do you want to change?

When working with families, Cerebra ask parents: what do you want to change about your child's sleep? Writing this down can help to focus on the problem – sleep issues can affect the whole household, including parents and siblings. There are four common sleep problems: difficulty settling, night waking, difficulty settling alone and early rising.

If the issue is around **difficulty settling**, think about whether the child's bedroom is suitable. Are the colours you have used on the walls too bright? It has been found that blue is the most stimulating

colour, along with green. In fact, blue light tells your brain that it is daytime so actually suppresses the melatonin produced. The red spectrum of colours don't stimulate the brain in the same way and therefore allow the melatonin to work. Also ask whether there are there too many toys in the room? Take them out if there are or put them away into cupboards or boxes. Does the child have a bright night light? Are they over-stimulated in their bedroom? You might want to use blackout blinds to reduce light coming in, particular during summer time.

Think about their bedtime routine and whether they are calm when they go to bed or are they excitable? Try to put them to bed when they are tired, even if it means doing so half an hour or an hour later. This may help reduce the time taken to settle and you can then gradually bring the time forward. Also think about whether they associate their bedroom with toys and playing. You might want to reinforce the bedtime routine by using visual timetables, something that dovetailed with what Nicki and Ben had mentioned earlier. The routine should take no more than one hour and a structured routine is very important. Do calm activities during this hour, switch devices like tablets off, give them a relaxing bath,

maybe a hand or foot massage and then put them to bed in a calm, quiet way, making sure the room is dark. It's worth noting that chocolate for example contains caffeine which is a stimulant and can remain in the body for up to 6 hours so avoid this close to bedtime.

One of the parents in the group suggested a book called 'The Rabbit Who Wants to Fall Asleep' as their family found it to be successful during the bedtime routine. Claire agreed that she had found it had worked well for some children.

It is worth considering that pain, discomfort, allergies and intolerances can all impact on sleep. It can be hard to know what is going on in children with communication difficulties and those with vision impairments may not be able to recognise when darkness falls. Sleep onset association disorder, when the child associates something sleep with a person or something in the environment, may also be an issue that will need to be considered.

Night waking is another significant issue and can be due to a number of factors. These can also include pain or discomfort so try to rule these out first as possible causes. Night terrors, nightmares and bedwetting can also be very significant factors for children of all ages and abilities. Think also about how you react when they wake up. 'Reinforced waking' can occur when the child gets some reward by your reaction. Try to stay calm and put them back into bed without talking too much or putting them in to bed with you.

Early rising, simply waking up too early, may be because your child simply does not realise that they should stay in bed or what you expect of them when they wake up. One possible strategy is to use visual clues for the child, for example a red light which if



Claire Varey from Cerebra presenting about sleep issues.

still on when they wake, shows them they should stay in bed. In the summer when it is light earlier, blackout blinds help to tell the child it is still night time and again, they should stay in bed.

Sleep Management

Claire said that before embarking on a sleep program, things parents are asked to consider including the following:

- Physical activity – is the child getting enough/too much/too early/too late?
- Is your child eating a healthy/balanced diet
- Medication – is this impacting on sleep? Could any changes be made?
- Are you using appropriate communication that your child understands and are you consistent?
- Are you ready/able to give consistent messages
- Are there any sensory issues
- Have you considered the needs of the whole family?

Unique's CEO Beverly Searle commented that sleep is a huge issue not just for families with KDVS but for lots of families with rare chromosome disorders. One parent in the group reported that they had had success with a 'gradual withdrawal' strategy, sitting on a chair next to their child's bed and then gradually moving the chair further away until they were eventually able to leave the room. This took a long period and lots of perseverance! Another parent said they had used a monitor that you can use to speak back to the child, to reassure them that they were safe and their parents were still there for them. The session concluded with a question from a parent about sleepwalking. Claire felt that as long as the child is safe, this should be fine. She explained that the brain is communicating with muscle groups during sleep and this is the likely cause of the sleepwalking.

Q&A with Dr Koolen

To round-off the day, there was a short question and answer session in which Dr Koolen took some questions. A discussion point was whether regular heart and kidney scans are necessary for those with KDVS. Dr Koolen felt that it is important to carry out the relevant checks when a diagnosis is first made but that if no structural anomalies are found at that time there seems little point in having regular heart scans. He did not feel an annual check would be necessary. This led to a question about checks for epileptic episodes and Dr Koolen's view was that it is important that parents are educated about the signs to look for when thinking about potential epilepsy so that they can then discuss with their child's paediatrician.

The next question was from a parent who had noticed a 'dimple' at the base of their child's spine. Dr Koolen said that it would be wise for paediatricians to investigate any potential issues with the spine and regarding the dimple that the parent had noticed, Dr Koolen felt that doctors would want to investigate whether the spine had closed properly at that point.

In response to other questions, Dr Koolen said that regular eye checks for those with KDVS are important to



monitor for any potential problems. He then answered a question from another parent, saying that he has no indication that KDVS is life-limiting (in terms of life span). This concluded the session but parents were asked to remain in the room for a very special finale!

Time to Dance!

When the session concluded, the young people from the Kool Club joined us to give a very special dance demonstration. They had been in a workshop led by Karen Bartholomew, working hard on an inclusive routine all day and everyone took part, from the youngest to the oldest. It was a wonderful demonstration, full of joy and happiness and the perfect way to round off the day.

A very Kool Picnic

To round off a very special weekend, on the Sunday some of the families, along with Dr

Koolen and his colleague Katrin had a family picnic in the grounds of Temple Newsam near Leeds. The weather was glorious and it was a lovely way for families to spend some time together before heading home.

Craig Mitchell, COO of Unique said, "It was fantastic to see so many families and their very special children at the event and a very humbling experience. We are very grateful to Awards for All, part of the Big Lottery fund, for providing Unique with the funding for this event, to Mandy Hazelgrave for her tireless efforts to organise it and also to the families who helped to fundraise to make it a reality."



Inform Network Support



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Join Unique for family links, information and support.
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entirely on donations and grants. If you can please make a
donation via our website at www.rarechromo.org. Please
help us to help you!

Unique would like to thank Mandy Hazelgrave for helping to
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information and for coming to the event. [CM] 2016

For more information, visit the Unique website at
www.rarechromo.org or the website for the research project led
by Dr Koolen at www.17q21.com/en/index.php.

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