

Ip36 study day Report

On a Saturday in early October 2009, twenty families with a child with a Ip36 deletion met – and for some it was their first meeting with other Ip36 deletion families. They, and *Unique*, were guests of Professor Chris Oliver, a clinical psychologist who is professor of neurodevelopmental disorders – that is, disorders that are associated with unusual development of the nervous system – at Birmingham University. Professor Oliver's team has mounted the first research study of the behavioural implications of Ip36 deletion syndrome and with trainee clinical psychologists Abby Marr and Dr Fay Cook, he presented the findings.

Unique welcomes children at its study meetings but as the Ip36 deletion day was held at Birmingham University, on this occasion they didn't attend. But from the youngest, aged 16 months to the oldest, aged 24, they were very much the focus of the day.

Ip36 deletion syndrome: an overview

Dr Louise Brueton, one of the team of consultant clinical geneticists at Birmingham Women's Hospital, introduced the day by giving a run-down on chromosomes and the key reported features of the Ip36 deletion syndrome.

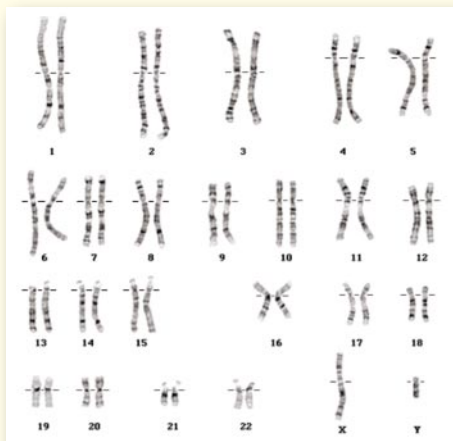
Dr Brueton told us that the first person with a deletion of Ip36 was reported in the medical literature in 1981 but at this time it was not recognised what this meant. A second person with a Ip36 deletion was reported in 1993 and then in 1997 the clinical features of Ip36 deletion syndrome were outlined. The syndrome is now estimated to affect 1 in 5000 people, making it the most common terminal (involving the end of the chromosome) deletion syndrome. However, as some children have very small deletions, around 50 per cent of those with a Ip36 deletion will have had a 'normal' chromosome test before the deletion gets picked up.

Chromosomes and DNA

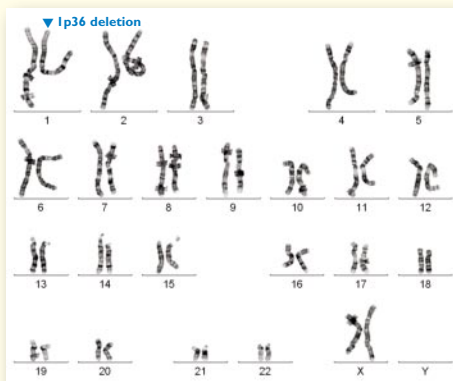
Our bodies are made up of billions of cells. Most of these cells contain a complete set of the estimated 20-25,000 genes. Genes act like a set of instructions, directing our growth and development and how our bodies work. Genes are carried on structures called chromosomes. In each cell (apart from the egg and sperm cells) there are 46 chromosomes, 23 inherited from our mother and 23 inherited from our father; giving us two sets of 23 chromosomes in 'pairs'. Apart from the two sex chromosomes (two Xs for a girl and an X and a Y for a boy) the chromosomes are numbered 1 to 22 generally from the largest to the smallest, meaning that chromosome 1 is the largest. As well as being the largest chromosome it is also

'gene-rich' (contains many genes) and harbours lots of important genes.

Fifteen to 20 per cent of children and adults with undiagnosed learning difficulties have 'subtle' differences in their chromosomes. These subtle changes are too small to be seen under the microscope but recent diagnostic tests known as fluorescent in situ hybridisation (FISH) and microarray comparative genomic hybridisation (array CGH) have enabled their detection. A very small deletion is known as a microdeletion. FISH can help detect a microdeletion, but only if the person ordering the test actually suspects that there is an anomaly of a specific region of chromosome Ip36. The newest test now available is an array CGH test. An array CGH test can detect a



A normal karyotype.



A karyotype showing a Ip36 deletion.



FISH analysis showing a Ip36 deletion.

Ip36 microdeletion from a single blood sample even when the doctor ordering the test does not even suspect this as a diagnosis.

Features of Ip36 deletion syndrome

Learning

All children known to have Ip36 deletion syndrome have learning difficulties, although the range of ability is broad:

- 88 per cent have a severe or profound learning disability
- 6 per cent have a moderate learning disability
- 6 per cent have a mild learning disability

Communication

Absent or delayed speech is common in children with Ip36 deletion syndrome. Around 75 per cent of children do not have speech, 17 per cent have speech that is limited to a few words and 8 per cent have two word phrases. Communication consists of more than just speech and this was covered in much more depth in the presentation by Jill Hoddell later in the day.

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Outlook

Over time there is a gradual increase in social interaction, motor skills and communication (both verbal and non-verbal).

Seizures

Almost half of those with Ip36 deletion syndrome are affected by seizures. The reported age of onset varies from 4 days to 2¾ years, although more than 50 per cent of those affected have had a seizure by the age of 2 to 3 months. Generally there is improvement with time in children's seizures although up to 20 per cent of children have seizures that are hard to control with medication.

Small head size (microcephaly) affects over three quarters of children with Ip36 deletion syndrome

Hypotonia (floppiness or low muscle tone) is very common in babies but generally improves with age

Behavioural problems have been reported in as many as 50 per cent of children (this was covered in much more detail by Professor Chris Oliver in a later presentation).

Brain anomalies

Many children with Ip36 deletion syndrome have a brain (MRI) scan and a number of anomalies have been seen:

- White matter (the channels of communication in the brain) changes in 28 per cent
- Prominent ventricles (fluid-filled regions of the brain) in 26 per cent

- Polymicrogyria (abnormal folding of the brain tissue) in 20 per cent

Heart defects are also common affecting over 70 per cent of children with Ip36 deletion syndrome.

Hearing problems are reported in around half of all children with Ip36 deletion syndrome.

Growth

Ninety-six per cent of babies are small for dates at birth. Some stay small but obesity can be a problem in a few children.

Eyes

A variety of eye problems have been reported.

Genital area

Minor anomalies of the genitals are common in children with Ip36 deletion syndrome, but particularly boys.

Thyroid

A small number of people with Ip36 deletion syndrome have an underactive thyroid.

Medical Evaluation and Assessment

It is recommended that all children with Ip36 deletion syndrome have the following medical assessments:

- A detailed cardiac evaluation including an echocardiogram (imaging of the heart)
- A detailed hearing assessment including a BSER (brain stem evoked response) test
- An ophthalmological (eye) examination

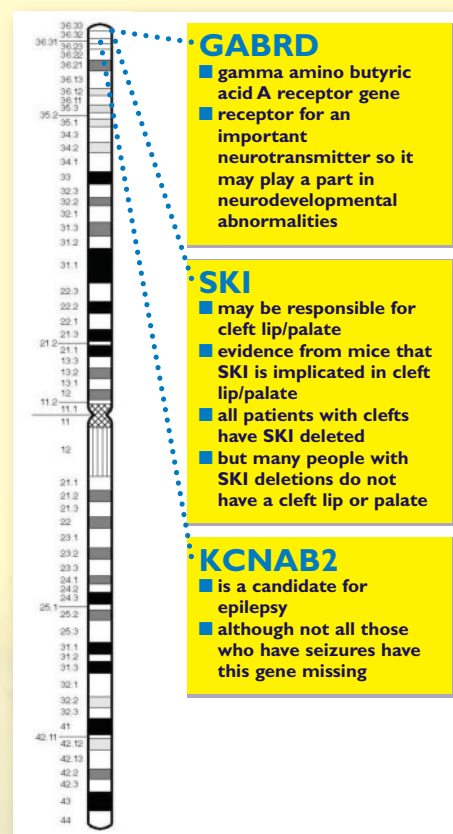
- Developmental assessment and monitoring
- A thyroid test
- A paediatric neurology assessment (for seizure management)
- Genetic counselling

Genetics of Ip36 deletion syndrome

In the vast majority of people with Ip36 deletion syndrome, the deletion occurred out of the blue (de novo) and was not inherited from the parents.

Potentially important genes

A number of genes that are located on chromosome 1p36 and may play a role in the features of Ip36 deletion syndrome have been identified:



The Ip36 behaviour study

Professor Oliver then presented the findings of his team's behaviour study. His team is particularly interested in difficult behaviours, how they come about and can be managed. In many ways children and adults with Ip36 deletion syndrome are just the same as everyone else and have the same needs, wants and rights as everyone else, and this should not be forgotten. He pointed out that even children with the same syndrome are unique and that there is huge variability from one child to another. But there are ways in which the children will be similar to each other and different from other children. At first the



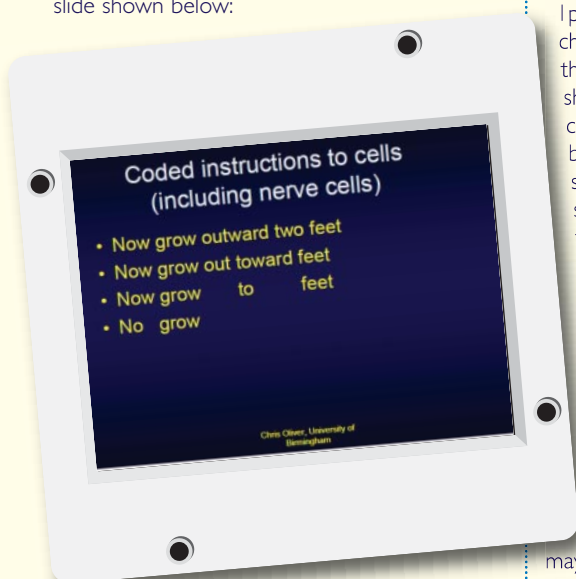


“There isn’t a cure but we can improve people’s quality of life by picking on particular areas and focusing on them.”

specific problems that go with any syndrome can seem overwhelming but once you start to break them down, you can make helpful changes.

Before the study, undertaken last year, Chris Oliver’s team identified concerns about the children’s sociability, the possibility of autistic spectrum disorders and also self injury. He stressed that self injury in 1p36 deletion syndrome is not inevitable and it doesn’t look severe.

Professor Oliver showed how a missing bit of chromosome can lead to tiny but important changes in the messages that the nerve cells in the brain receive. The message doesn’t need a very big change for its meaning to be completely scrambled, as demonstrated in the slide shown below:



“It’s not that a particular syndrome or disorder leads to a particular behaviour. The information flow that comes in gets disrupted.”

Sociability and the possibility of autism

Dr Fay Cook, now a qualified clinical psychologist, reviewed the behaviour study. Twenty-three families took part, each completing 11 questionnaires. The youngest participant was one year old, the oldest 16 (with an average age of 9 years). One in 10 was fully mobile; 52 per cent were partly mobile. Thirty-five per cent had normal vision and 61 per cent normal hearing. Thirty-nine per cent had some speech, varying from vocalisation to full sentences; and 17 per cent

had some self help skills like dressing, feeding or washing.

The researchers found that more than a quarter of the children – 27.3 per cent – had an abnormally low mood, often associated with health problems. By contrast, 9.1 per cent had elevated mood.

Overactivity was not common, occurring in just 4.3 per cent of the children, while almost one in eight was impulsive.

From the questionnaires completed by the parents, it seemed that the children were indeed sociable, but more so with familiar people than with a stranger (which you might expect). The children’s scores on social communication put just over half of them within the range for autism or autistic spectrum disorder (ASD) but their repetitive behaviours were less striking.

The researchers thought that these traits – lowered mood, higher sociability with familiar adults, impaired social communication – might form a behavioural pattern specific to the 1p36 deletion, so they visited twelve of the children, from the ages of 3 to 13, to see for themselves. This so-called observational study showed them that in very specific situations children responded in a very similar way to both familiar and unfamiliar people. Not surprisingly, children were much more sociable when people actively engaged with them although they observed that children’s attention was often more focused on toys than on the people themselves.

Overall, they concluded that children are really quite sociable, showed very little distress, had good social skills and wanted attention, so they were motivated to be sociable.

What does this mean? They did not find a high level of autism although some autistic features such as less eye contact may be caused by features of 1p36 deletion syndrome. Children with problems with their eye muscles found it harder to move their eyes and to establish eye contact.

Enhancing social skills

- Remind your child to look at you when interacting
- Give praise for using social skills
- Tell others that children like a lot of attention and interaction
- Give rewards

Self injury

Abby Marr, who has also recently qualified as a clinical psychologist, looked at self injury among this group of children with a 1p36 deletion. She defined it as ‘any behaviour initiated by the individual that directly results in physical harm to that individual’. Typical examples would be

hand biting, hitting themselves or hair pulling. Self injury, she said, is shown by 4–12 per cent of children with severe intellectual disabilities.

She explained that it can start when children are very young (under 5 years of age) and become a longstanding problem and that there is an association between certain genetic syndromes and a risk of developing self injurious behaviour. Self injury is an important behaviour to explore for both identification and intervention. Triggers include the wrong level of attention – either too much or too little – and the child being asked to do something too stressful or demanding.

Out of twelve children who were visited, six showed self injurious behaviour. Four showed hand biting or sucking. Three of them showed it when they were being ignored (had low attention and interaction); and three when they were being engaged with. So the researchers found that the environment has an influence on children’s behaviour. The other factor that came out of this study was that children would move towards or away from an adult and therefore showed signs of communication. This is very important for the treatment of self injury as sometimes these signs of communication can later develop into self injury. If it is possible to work with children on these communication behaviours, we may be able to prevent self injurious behaviour.

In summary

Chris Oliver summed up the conclusions of the behavioural research.

“We don’t think ASD is a big part of the disorder. They score high in certain areas because of their greater degree of disability. That’s very positive alongside the sociability because it means that dealing with behaviour problems is easier.”

It is important that one in four children show an abnormally low mood. The researchers saw aggression in half of the children, but with no intent to harm. Aggression, he pointed out, is normal for children but can become a problem.



Self injury, pain and discomfort

Of the 14/23 who were self injuring, the most common way was self biting, but one in three were hitting themselves or their heads.

To address self injury, he first advised parents to ask themselves if their child was in pain or discomfort. If the difficult behaviours do not vary with the environment, he said that parents should think pain.

He wondered whether low mood is associated with self injury and with pain and discomfort. Among typically developing children, one in eight headbangs at night and of those half have middle ear infections. So parents must really get on top of common health problems like middle ear infections and tooth decay.

He wondered whether reflux was more of a problem in children with 1p36 deletions than commonly acknowledged. Reflux is related to middle ear and sinus problems and through tooth erosion to tooth decay. He also

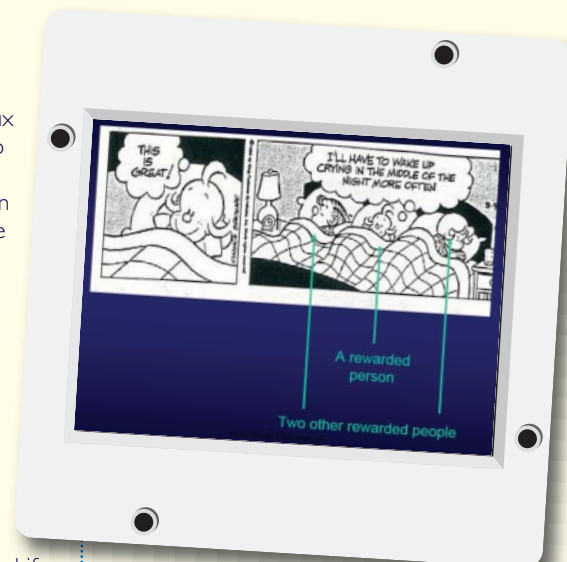
wondered whether when children had their fingers in their mouth they had reflux (feeds and stomach acid return readily up the food pipe from the stomach) causing pain and discomfort which can manifest in behavioural associations. The pain that the reflux causes and attempts to relieve this pain can result in fidgeting, hands or fingers in the mouth, excessive salivating, an arched back or grinding of teeth. Children with reflux may also be more likely to self-injure and the pain may be an important indication of why they do so. The pain caused by the reflux can be blocked ('gated') by rubbing, scratching or hitting another part of the body. He suggested that parents ask for a GP referral to a gastrointestinal specialist – and if necessary, sit on the GP's floor and refuse to go until they have a strategy to deal with the problem.

Each child has specific behaviours associated with pain, known as a 'pain signature'. He suggested that parents try to recognise their child's pain signature and compile a DVD of their child's behaviour when in pain for their school and other carers.

Professor Oliver pointed out that once a particular behaviour starts for a reason (such as teething) it can acquire a function. It causes adults and carers to respond. For children who have a problem communicating, the behaviour becomes useful for them as a means of communication. If the behaviour makes someone give the child social contact, that can be a reward and make it more likely to occur again. It has then become learned behaviour and may need addressing through the clinical psychology service.

“Stop and think ‘One, two, what shall I do? If I do something, will that be a reward for that behaviour?’”

To prevent a child using self injury as a means of communication, Professor Oliver stressed using other means of communication and how important it is to teach effective early communication.



“A child with an intellectual disability has far fewer ways of communicating. But 1p36 children will find a way to show what they want.”

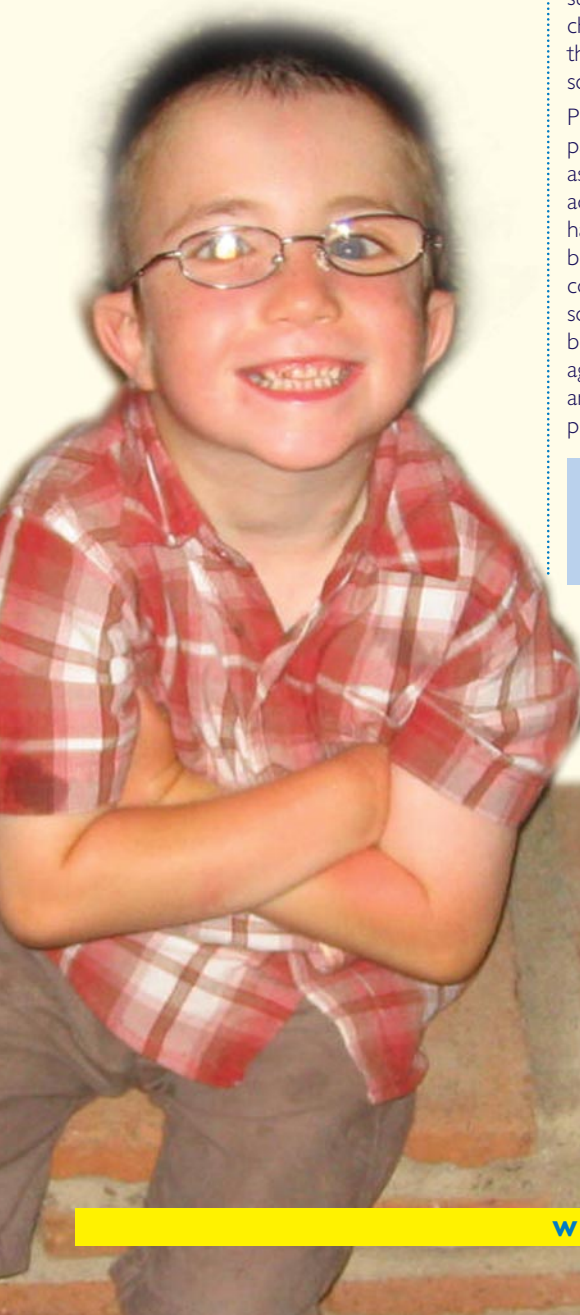
Experiences of getting a diagnosis

Ruth Fishwick, now a newly qualified clinical psychologist, described eight mothers' experiences of receiving the diagnosis of 1p36 deletion syndrome for their child. The families included four boys and four girls with 1p36 syndrome and the children were aged between three weeks and four years at diagnosis. At the time of the interviews the children were aged between 20 months and 11 years.

One of the reasons for conducting this study was that there is very little information in the published medical literature about parents' experiences of receiving a diagnosis. But what there is in the published literature, including a study of *Unique* families with a child with a 4q deletion, suggests that parents feel distress and grief, they are troubled by the lack of information and have a sense of being unsupported by professionals. On the positive side, they are relieved to have an explanation for their child's problems.

Mothers told Ruth that they felt professionals were negative about the diagnosis and they themselves felt powerless. These feelings stayed with them. They were uncertain about the future, their child's life expectancy and possible abilities. Would their child ever become independent? What stage would they get to? Would they have children of their own? Mothers wanted information immediately but the professionals didn't know. This increased their sense of worry and fear because information does help to get over the uncertainty. These negative feelings were partly counterbalanced by a sense of relief at getting a diagnosis and getting access to services.

Did the diagnosis make a difference? Some families had lived with their child's disability for





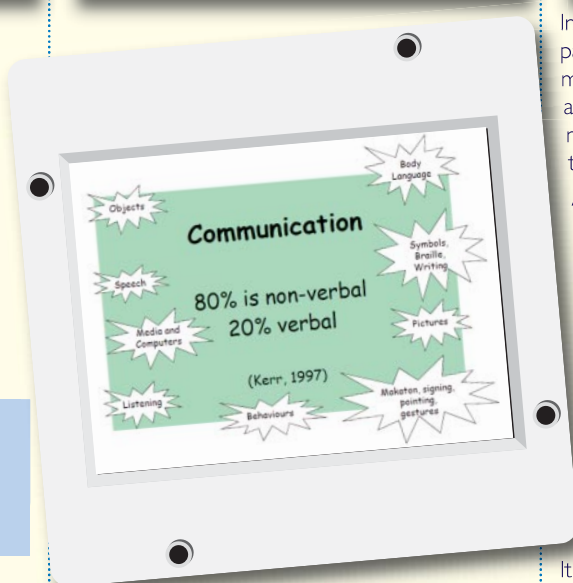
years and the diagnosis didn't change their difficulties. For others knowing made a difference; other family members needed to know if the disability was hereditary or not. One further benefit from receiving a diagnosis was access to relevant support groups and organisations.

Ruth's aim now is to get the message out to professionals about how families really feel when they get the diagnosis of a genetic disorder in order that the experience of receiving a diagnosis can be a more positive one.

“There are plenty of wrong ways of doing this but no right way. The world disintegrates around you and then you get back on your feet.”

Communication, speech and language

Jill Hoddell, a retired speech and language therapist who has recently joined Professor Oliver's team, talked about communication.



She defined communication as the ability to exchange information and ideas and to influence the environment by any means possible and stressed that it is a two-way process. Eighty per cent of it is non-verbal and only 20 per cent verbal. Any behaviour has the potential to send a message, she said: we have an innate desire to communicate.

For communication to take place, you need a good environment, a shared system, someone to communicate with and time to process and give information.

Things that can get in the way of communication include lack of need or opportunity to communicate; hearing and visual impairments, attention and memory difficulties; and information overload.

In addition, facial structures such as a high palate and weakness in the facial muscles can make it hard to put words together. So there are many reasons why communication may not be occurring and a speech and language therapist needs to investigate.

Attention and listening is essential for all forms of learning, especially for language learning. Attention includes keeping interest, copying and listening and eye contact. It also involves the ability to turn off or ignore external stimuli which is a skill that must be learnt. Attention difficulties impede both language and social communication. The ability to hold attention develops over 5 to 6 years from early distractibility to an ability to focus and concentrate. The wrong environment can distract attention, as can feeling unwell, being tired or getting over a seizure.

It is easier to understand in context or with a visual or object prompt.

If pressure is put on the communication environment, it's very easy to give up if it's too effortful. A child who gives up communicating may become very passive. Alternatively as discussed in the previous session with Chris Oliver, children may use challenging behaviours to express a need or as a direct result of frustration due to comprehension difficulty. Therefore behaviours can be a symptom of an underlying need or difficulty rather than itself being the difficulty. People tend to use too much language and not bring communication down to the child's level.

How can you help?

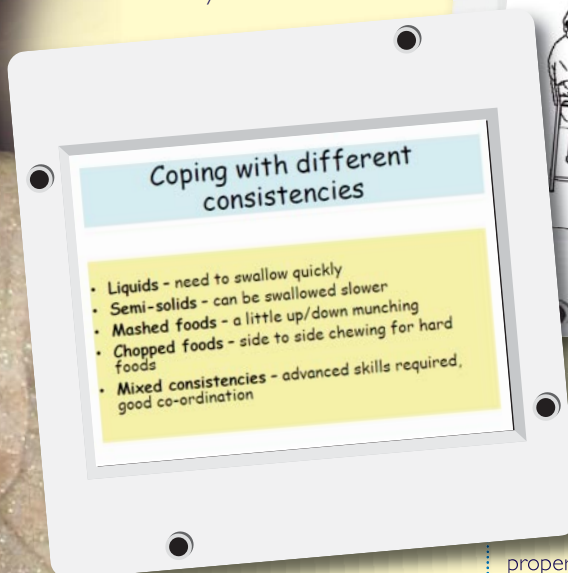
Time is a concept that's hard to understand. You can help a child to anticipate what's coming by having a timeboard or routine. The environment is crucial; if it is too noisy or distracting a child may find it difficult to concentrate. It is easier to communicate if you keep noise low, turn the TV off and get the lighting right. It's easier to understand one-to-one than in a group.

So get the child's attention first, holding their face if need be. Once the child is focusing, you can deliver your message. When delivering the message try to monitor the language you use and keep it at an appropriate level. You can reinforce language with different tones,





and in making the mouth movements needed to eat mashed and chopped foods, while mixed food consistencies need very advanced skills. Children can also have difficulty calculating how much to eat, handling cutlery, co-ordination and staying in the right position to swallow effectively.



gestures, objects and pictures. Using objects of reference helps people to understand. You can build up an object of reference timetable box to chart the progress of the day. If articles are presented just before the activity, with persistence and over a period of time a child will begin to associate the activity with the object.

Jill then discussed alternatives such as picture symbols and sign systems such as Makaton, a more gestural form of British Sign Language. To convey your meaning you can use a real object; part of the object; a photograph; a colour picture; a black and white drawing; a symbol; or a written word.

To summarise Jill talked about the 'positive spiral of communication'. When there is a positive environment for communication, communication becomes increasingly successful which leads to an increased motivation to communicate and therefore frequency of communication also increases.

Eating and drinking

Jill Hoddell talked about swallowing disorders, known as dysphagia. They can be caused by neuromuscular or anatomical difficulties and can cause aspiration when food goes down the wrong way. Persistent aspiration then increases the risk of aspiration pneumonia.

Eating and drinking is an everyday activity that we take for granted. It is usually automatic and is a social activity. For children with 1p36 deletions, there can be difficulties in swallowing liquids which have to be swallowed very fast

Muscle weakness makes keeping food in the mouth hard and chewing difficult. Some children have a lack of sensory awareness of having food in their mouth or by contrast hypersensitivity to food in the mouth.

Signs of difficulties include: lots of dribbling; coughing with a drink; chestiness after a drink; food pouching in the cheeks and even losing weight.

Children who cannot yet swallow normally and cough when they drink can have thickened fluids to slow down the rate at which they must swallow. They need to be seated in a good position with their head supported, their neck elongated and their chin tucked in.

Finally, Jill said that dysphagia teams are being rolled out across the country and families who would like a referral should ask their speech and language therapist or their GP for a referral.

Questions on eating and drinking

Families shared their experiences on encouraging a child to take lumpy food. Jill pointed out that a child with a high palate may have difficulty moving food around the mouth with their tongue and getting food ready to swallow. She said that some children just take that bit longer to get used to new textures. But she also told a family with a 16-month-old who wouldn't tolerate anything with lumps not just to wait acceptingly for their speech therapy appointment but

to ring up and nag until they get put to the 'top of the pile'. The mother of a 13-year-old said comfortingly that when her daughter was younger, everything had to be smooth but from the age of 5 to 6, she had eaten proper food.

Another family asked if their daughter, who had previously eaten normally but has been fed entirely by gastrostomy for two years due to aspiration, would ever eat again. Although she is much stronger, she has become phobic about food and even having her teeth brushed. Jill and Chris Oliver agreed that she needs to work with behavioural psychologists and speech therapists on a desensitisation programme to gradually fade oral feeding in.

