Unique

Pallister Killian Syndrome

A note

Information in this leaflet comes both from the published medical literature and from the experience of Unique. Thirty-two families affected by PKS were surveyed by Unique in 2004; information from this survey is marked (U). Unique is extremely grateful to the families who took part in the survey.

References

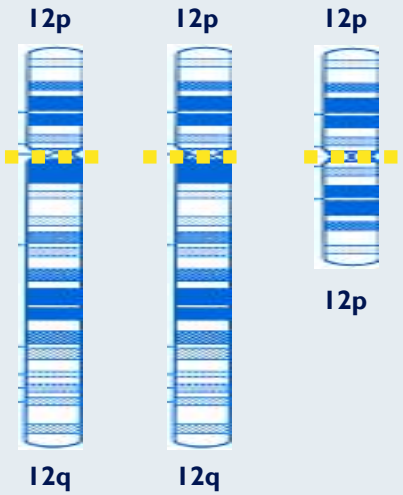
Throughout the text there are references to articles published in the medical press. The references are grouped at the end of paragraphs. You can search for the abstracts or original articles in PubMed or obtain the full list of abstracts and key articles from Unique.

Pallister-Killian Syndrome or mosaic tetrasomy 12p?

Mosaic tetrasomy 12p is a rare chromosome disorder. It is caused by having a small extra chromosome made up of two copies of the short (p) arm of chromosome 12 in some cells of the body. In these cells there are four copies of this arm of chromosome 12 instead of the usual number of two.

The effects of mosaic tetrasomy 12p are caused by the genes carried on the extra chromosome. Typically, these genes cause a distinctive syndrome called Pallister-Killian Syndrome (PKS). However, among people with mosaic tetrasomy 12p the severity of the effects varies enormously. The reason for these differences is not well understood, but while all affected children have mosaic tetrasomy 12p, only those who are recognisably affected can be said to have PKS. This leaflet describes those children who have Pallister-Killian Syndrome.

Chromosome disorders are usually diagnosed by examining white blood cells. However, people with mosaic tetrasomy 12p often appear to have normal chromosomes in their blood cells, so the diagnosis is usually made from skin cells or cells taken from inside the cheek.



Main features

- Marked floppiness (hypotonia) in babies.
- Developmental delay.
- Learning difficulties.
- Delay in developing speech or absence of speech.
- In babies and young children, a distinctive facial appearance, including a high, rounded forehead, broad nasal bridge, widely spaced eyes and a large mouth with a thin upper lip and a 'coarse' look to the face.
- Sparse hair or bald patches around the temples, filling in by around 5 years, and thin or sparse eyebrows.
- Streaks or patches of darker or lighter skin, obvious at birth or emerging later.

Although these features are highly suggestive of PKS when taken together, no child has all of them. The only way to be certain of the diagnosis is to examine the chromosomes.

Other typical features

- High arched or cleft palate (roof of the mouth).
- Short arms and legs, out of proportion to the body.
- Diaphragmatic hernia (a hole in the muscular wall separating the heart and lungs from the other contents of the abdomen. Part of the bowel, stomach or liver take up space in the chest, potentially depriving the lungs and heart of room to develop properly).
- Seizures.
- Sensorineural (permanent) hearing loss.

Many other features have been found in babies with PKS. These include heart defects, extra nipples (and an extra breast in an adult), feeding difficulties and gastro-oesophageal reflux (a condition where feeds flush readily back up the food pipe), large big toes and extra fingers, epicanthal folds (skin folds across the inner corner of the eye), and a large tongue that develops after babyhood.
Some features of PKS overlap with those seen in trisomy 12p (where people have three copies of the

Other names

*The name **Pallister-Killian** goes back to the doctors who first described the syndrome. In 1977 Dr Philip Pallister, an American paediatrician and geneticist, first described two adults with PKS while in 1981 an Austrian doctor Wolfgang Killian described four more people with it. PKS is occasionally called **Teschler-Nicola/Killian Syndrome**, recalling Dr Killian's fellow worker Dr Maria Teschler-Nicola.*

*The name **Tetrasomy 12p** simply means four copies of the short arm of chromosome 12 and the name **Isochromosome 12p** tells you that the additional chromosome (12p) is made up of two mirror copies of itself.*

***Mosaic** tells you that cells with the extra chromosome exist side by side with cells with a different number or arrangement of chromosomes.*

Families say …

" *His smile can light up the world. Yet the diagnosis was so blunt I thought I would lose him at any moment.*

Typical hair pattern

The typical PKS hair pattern is of sparse hair or bald patches over the sides and top of the head. The great majority of babies are affected, but not all. Eyebrows are also typically thin or non-existent and even eyelashes may be sparse. The hair pattern may not be seen at birth but become obvious within months. By mid-childhood, hair grows so the PKS pattern is no longer visible.

short arm of chromosome 12) such as a high or prominent forehead, a flat nasal bridge, a small upturned nose, full cheeks, a long philtrum (the tissue between the nose and the upper lip), small broad hands with broad fingers, bushy eyebrows, a projecting broad lower lip, a round face and small, low ears.

Other features are typical only for people with four copies of 12p, such as thin hair growth, sparse eyebrows, a large mouth and in some people the patches of darker and lighter skin (Leube 2003; Genevieve 2003).

How common is PKS?

Unique has 30-35 members worldwide. By 2001 over 100 people had been described in medical articles (Dufke 2001).

The diagnosis can be difficult to make and it is not known how many people have not been diagnosed. The recent emergence of people with mosaic tetrasomy 12p with little or no learning difficulty or other signs means that the true prevalence may never be known.

First signs

The facial characteristics of PKS include a square head with a prominent forehead, upwards slanting and wide-set eyes with epicanthic folds (skin folds across the inner corner of the eye), a broad, flat nasal bridge and a wide mouth with a prominent upper lip.

Although these characteristics are quite typical, they only suggested the correct diagnosis in two out of 12 children in the *Unique* series. Other signs in babies diagnosed as a result of unusual features at birth were profound hypotonia (floppiness), jaundice, skin discoloration, cleft palate, short arms and legs, extra fingers and/or toes, other unusual features of the hands and feet, such as talipes (club foot) and congenital hip dysplasia (abnormal development of the hip joints that is present at birth). Six babies were only diagnosed after showing developmental delay, two when they made no eye contact by their 6-week baby check and three others who failed developmental assessments at six and nine months (U).

Typical skin patterning

Streaks or patches of lighter or darker skin are highly typical of mosaic tetrasomy 12p, as of other mosaic chromosomal disorders. The under- or overpigmented skin can occur anywhere – on the body, legs, knees, arms or less commonly on the face. In children with mosaic tetrasomy 12p without typical PKS, it may be the only visible sign. The discoloured skin is not always visible at birth and in some children only becomes obvious after sun exposure.

Diagnosis: prenatal diagnosis

First signs in pregnancy

A diagnosis during pregnancy usually follows concern about fetal development or detection of an anomaly. While some pregnancies with mosaic tetrasomy 12p are unremarkable, polyhydramnios (*see right)* has been described both in the presence of structural defects and when they are not present. Typical anomalies in pregnancy are short arms and legs, a diaphragmatic hernia, increased nuchal translucency (the thickness of the fold at the back of the neck) and heart defects. A small head, otherwise common in chromosome disorders, has not been observed. One team of researchers believes that typical facial features (small nose, thin upper lip and lower one) can also be detected by mid-pregnancy ultrasound (Mathieu 1997; Schaefer 1997; Langford 2000; Paladini 2000).

Diagnosis in pregnancy

Diagnosing any mosaic condition is difficult because of the neighbouring populations of normal cells and cells with a chromosome anomaly. During pregnancy, mosaic tetrasomy12p can sometimes be confirmed from a sample of chorionic villus (CVS) tissue taken from the developing placenta around 10 weeks after fertilisation. CVS cells develop from the same fertilised egg as the embryo (developing baby) and usually share the same DNA (genetic codes). However, the CVS cells do not always reflect those in the baby and this test may miss the diagnosis. If the baby's features suggest PKS but the CVS result comes back negative, an amniocentesis is needed.

What is polyhydramnios ?

Polyhydramnios *means there is an unusually large amount of amniotic fluid. There are many possible causes and your unborn baby will have a detailed ultrasound scan. Too much amniotic fluid can lead to premature delivery and 6/18 Unique babies with mosaic tetrasomy 12p were born early. Growth retardation has not been reported in the Unique series. On the contrary - many babies are large for dates.*

Less commonly, babies have been found with ***hydrops****. This is a severe bloating of the baby's tissues, caused by excess fluid due to the baby's inability to manage fluid and is risky because it can overwhelm the baby's organs.*

(Schinzel 1991; Langford 2000; Paladini 2000; Dorey 2002)

Chromosome diagnosis on cells obtained by amniocentesis is usually accurate, especially if FISH using a chromosome 12 centromeric probe (a special test that picks up signals from the centromere) is used to increase certainty.

However, it is not possible to distinguish mild cases from severe ones just by looking at the chromosomes in pregnancy (Bielanska 1996; Schaefer 1997; Doray 2002;Dong 2003;Polityko 2004; Vekemans personal communication).

Diagnosis after birth

In babies and children, PKS is usually diagnosed after birth when concern arises either over birth defects, appearance or over later development. Chromosomes from a blood sample are usually examined first, but in PKS this often produces a normal result. This is because in cell types that have a rapid turnover, such as white blood cells or bone marrow, the cell line with the extra chromosome tends to be lost in favour of the cell line with normal chromosomes. A blood sample taken within days of birth may, however, still reveal some tetrasomic cells. Tissues with a slower cell turnover such as skin or the mucous covering of the inside of the mouth (a buccal smear) are more likely to reveal the additional chromosome for longer (Manasse 2000).

When you are told your baby's karyotype (chromosome make-up), you will probably also be told what proportion of cells contain the extra 12p chromosome. It is not wise to read too much into this, as this result does not reflect the overall proportion in the body. In particular it does not reflect the proportion in the vital organs, such as the brain, at critical stages of development before birth.

Late diagnosis occurs commonly and many families experience false dawns with apparently normal results from chromosome analysis before the extra chromosome is found. Among *Unique* members, the search for a diagnosis usually took months and for many families it took years. One baby was diagnosed at 5 days (and was the only baby to show the extra chromosome in blood cells) but many were not diagnosed until 2 to 3 years of age.

Mosaic tetrasomy 12p: what can it mean for my baby?

Mosaicism for any chromosome disorder makes predicting a child's outlook very difficult. This is particularly true for babies diagnosed before birth, where the additional chromosome has been identified without any clear indication of whether the baby will or will not have typical Pallister-Killian syndrome and if so how severely. Ultrasound scans can reveal physical problems but cannot tell you about a child's future cognitive ability, their character or how high a quality of life they will lead.

Once your child has shown their individual pattern of development it will become easier to predict their longer term possibilities. Older medical texts from the early 1990s tend to paint a gloomy picture. While it is true that some children will be very delayed in walking if they achieve this at all and will not talk, others may only have mild learning difficulties or none at all. However, mildly affected children are probably rare (Schinzel 1991; Doray 2002).

Among adults, the level of physical disability differs considerably, with three people known to *Unique* able to sit and walk while two others are not mobile. All the adults described in the medical literature or known to *Unique* have a learning disability (Horneff 1993, U).

Very occasionally, children are born who have a more complex rearrangement of their chromosomes. There have been published reports in only three children so far of tetrasomy/trisomy/disomy mosaicism, but their outlook appears to be somewhat better (Leube 2003).

What to expect in pregnancy and at the birth

While pregnancy is often problem-free, complications can develop. One of the most common is polyhydramnios (see page 5) and premature birth is common, in *Unique*'s experience from 29 weeks onwards. Babies are usually a good size and weight at birth and some are large, with a notably large head circumference. Despite this, low Apgar scores are common and most babies are profoundly hypotonic (floppy) at birth. Typically, they experience distress, needing resuscitation and in most cases care in the neonatal intensive care unit. Their breathing is commonly affected, so they need additional oxygen and some need to spend at least a short time on a ventilator.

Many babies are reluctant to feed, partly because the sucking reflex is not developed or because newborn babies with PKS find it difficult to co-ordinate sucking, swallowing and breathing. These difficulties may be exacerbated by the typically high arched palate or, in some babies, a cleft in the soft or hard palate. Occasionally babies may have a cleft in the uvula (the extension of the soft palate that hangs from the roof of the mouth above the back of the tongue) (U).

At birth a typical baby with PKS has a specific facial appearance: a large, square head, a prominent, rounded forehead, a high hairline with apparently receding, scant or patchy hair, thin or scarcely visible eyebrows (and eyelashes); low-set ears; widely spaced upslanting eyes with skin folds at the inner corners and a flat bridge to the small, snub nose, chubby cheeks, a large mouth with a prominent upper lip and a long space between the nose and mouth, a large and sometimes protruding tongue, a small chin and a short neck.

Other visible features you may notice include the disproportionately short arms and legs, with small, broad hands and feet, short and tapering fingers and toes with underdeveloped nails. Some babies have an extra nipple.

How can PKS affect growth?

Babies with PKS are generally large at birth. The baby's size may be evident before birth, so that mothers are frequently warned to expect a large baby. Among twenty babies in *Unique* whose birth weight is known, average weight was 3684 grams (8lb 4oz) and the two heaviest babies weighed 4650 grams (10lb 4 oz) at birth, while the lightest in this group weighed 2891 grams (6lb 6 oz). One baby, born at 29 weeks, weighed 1276 grams (2lb 13oz). Another baby with PKS described on a PKS e-

Families say …

"*At 7, Federico is too hypotonic to stand alone or to walk – but he does ride with his pony instructor.*

"*Physically, Phil was an early developer, sitting at 7 months, crawling at 12 months and walking alone at 22 months. At almost 8 years, he runs, swims, cycles and plays football.*

"*Eleonore, who is 14, has walked since she was six years old. Today she swims, walks, abseils and canoes.*

"*At 16, Joshua rides a tricycle. His persisting hypotonia makes it more difficult for him to walk and run and particularly to get up from the floor.*

group weighed 4960 grams (10lb 15oz) when he was born at 34 weeks and by the age of 10 weeks weighed over 7 kilos (15lb 7oz). Other PKS babies have also been described as being both large and tall, although in some children the limbs are disproportionately short. By adulthood, the growth advantage tends to be lost, so that most adults with PKS who have been described are short (Genevieve 2003).

How can PKS affect a child's overall mobility?

The hypotonia that affects babies from birth tends to persist at least into early childhood, and babies with PKS are delayed in reaching their motor development milestones. The range of delay is very varied, with the age at which children in the *Unique* series first sit up or roll over and become mobile ranging from 6 months to 5 years. The age at which children take their first steps varies between two and six years and some children need supportive footwear, splints, standers and walking aids to achieve this. Although babies are late to roll and sit up, some ingeniously learn to scoot on their backs. In general, babies who sit early tend to walk early and go on to become more fully mobile than babies who do not sit until four or five years. However, even late sitters and walkers and those who never walk can take part in a broad variety of sports activities. Overall, it has been stated that 30 per cent of children and adults with PKS are able to walk (Mathieu 1997).

In many children the early hypotonia improves with increased mobility but as it does so, it may be replaced by increased muscle tone. Some older children may also develop joint contractures and others may develop the spinal curvature of scoliosis (Horneff, 1993, U).

How can PKS affect a child's ability to learn?

Most children with PKS experience learning difficulties and experience so far suggests that for many the disability is marked and is exacerbated by hearing and vision problems. However, some children have only a mild learning difficulty. It is not possible to predict before birth which children will be more severely or mildly affected, but abilities will become clear through the early years. Most children attend special schools but some are in mainstream schooling with a dedicated support worker or teacher (U).

How can PKS affect communication?

Speech tends to be late to develop and may remain limited or not develop at all. Many families report a lack of eye contact and communication in the early years and a tendency for their child to live in a separate world of their own. However, in the pre-school years most children communicate their likes and dislikes with vocal noises and gestures and may understand simple requests and statements. Older children benefit from tactile signing and assisted communication devices. The link between the ability to speak and to learn appears to be strong as among the older children the three most versatile learners also speak most fluently.

Children learning, families say …

- *Joshua loves to draw and always tries to draw something if he can't explain it. He reads large print and can write simple sentences but finds it a struggle and prefers to use his computer. He has an excellent memory and overall is better at practical tasks. He enjoys art and pottery as well as computers. His learning difficulties are severe* - age 16.
- *Eleonore reads occasional words and writes her name with help. She has been able to use a keyboard from 10 years and her strengths are computer skills and music. She also has an excellent memory. Her learning difficulties are described as severe* - age 14.
- *Phil started to read this year. Today he reads school books and children's books and writes short to medium length sentences. He has a good memory and his strengths are visual memory and logic. He attends a mainstream school with a support teacher. His learning difficulties are described as moderate* - age 7.
- *Lauren has profound learning difficulties but she has a good memory and at the age of 7 remembers songs sung to her as a baby. She is always improving, but very slowly* - age 7.

Children communicating, families say …

- *Joshua started speaking at 5 years. Before that, he spoke only odd words. Today he uses long and complex sentences.* Joshua is 16.
- *Eleonore learned sign language at first and has only used proper speech in two to three word phrases in the last few years. At 14, she is still hard to understand and finds consonants very hard to say. She understands most of what we say with the help of signing but can only express her wants and occasionally her dreams, such as 'I want to go on a plane!'*
- *Kerstin communicates through mimicry and vocal noises we have learned to interpret. We are not sure how much she understands.* Kerstin is 13.
- *Phil has good understanding but more limited expressive ability and his large tongue and jaw impede his clear speech. At 7, he speaks in 5 to 8 word sentences.*
- *Lauren will pick up sweets or a drink placed in front of her and will push or throw away objects placed in front of her. She does not speak.* Lauren is 7.

Medical concerns

Apnoea

In *Unique*'s experience, many newborn babies experience apnoea (a temporary stop in breathing) and some need long term assistance with their breathing. Some babies come home from hospital on oxygen and apnoea monitors and many parents use monitors overnight. The underlying hypotonia affects the windpipe, making it softer and more liable to collapse. A small number of babies need a tracheostomy (a tube known as a 'trach' tube inserted into the windpipe to allow air and oxygen to reach the lungs). As babies mature, their muscle tone improves and they can be weaned off respiratory support.

Diaphragmatic hernia

This is a specific defect associated with PKS (see p3). As a consequence, the baby's lungs and to some extent their heart, are displaced and may not have enough room to grow. All babies in whom this defect can be repaired need early surgery. Some babies may die in the neonatal period but in others the surgery allows the cramped lung or lungs to grow, although full size may never be reached. For more information, see www.ich.ucl.ac.uk/factsheets/diseases_conditions/diaphragmatic_hernia

Genitals

Slight abnormalities of the genitals are fairly common although they usually do not need surgical repair. In girls the anus and vagina may be found to be unusually close together (anterior displaced anus), while in boys the genitals may be very small and the testes may not have descended into the scrotum. An operation to bring them down and anchor them may be recommended. An occasional finding in girls is a closed vagina. A closed (imperforate) anus has also been reported.

Seizures

Seizures affect almost half of the children with PKS known to *Unique* and are described even more frequently in the medical literature. They may start in babyhood, in childhood or not until puberty.

Seizures types vary, with nocturnal seizures reported by a small proportion of families. Families do not perceive a link between seizure activity and their child's ability to learn, and all the children with reasonably fluent speech also have seizures. In one case they are also hard to control (Horneff 1993; Mathieu 1997; U).

Brain

Babies and children diagnosed with PKS can expect to have a brain imaging investigation to establish whether the brain has been structurally affected by the chromosome disorder. The two cerebral conditions reported most frequently in the *Unique* series are atrophy (where the brain is smaller than expected) and hydrocephalus (an excess of cerebrospinal fluid in the brain), but these affected just a third to a quarter of the children (Horneff 1993; Mathieu 1997; U).

Heart

The additional chromosome may have an effect on the development of the heart, so all babies will have a thorough cardiac investigation. Overall, a quarter of babies with PKS are born with a heart condition, most commonly a ventricular septal defect (a hole in the wall between the two pumping chambers of the heart) or an atrial septal defect (a hole in the muscular wall between the two filling parts of the heart). Treatment depends partly on the size of the defect and while some holes will close naturally in time, large defects may need surgery. Persistent ductus arteriosus also occurs (the channel between the aorta and the pulmonary artery that takes blood to the lungs and usually closes shortly after birth remains open instead). The aorta itself may be narrowed, as may the valve that leads from the heart to the aorta. It may be possible to expand the narrowing surgically (Schinzel 1991).

Spine

The full examination of a baby with PKS will include imaging of the spine. While most children in the *Unique* series have no spinal abnormalities, a small number of children have a degree of spina bifida, due to incomplete development during fetal life of the spinal column. None of the *Unique* series has an open spina bifida, but one child has the occult form and another has a tethered spinal cord, in which the cord is abnormally stretched and surgery is recommended to prevent neurological deterioration.

While in spina bifida occulta the spinal cord is usually intact, in some children there is a loss of sensation affecting the lower limbs and bowel and bladder control.

Some babies develop a spinal curvature during childhood (scoliosis or kyphosis) and require adapted seating, bracing and sometimes surgery to straighten the back.

Hands and feet

The typical PKS features affecting the hands and feet are an extra finger (sometimes with an extra toe, as well) and sometimes a large and broad big toe. Another sign is unusually short hands and/or feet. In the *Unique* series, many other unusual hand features are also described: clenched, curved, stubby or tapered fingers, long thumbs and in one older child, the development of coarse skin on the hands. One child in 10 has a degree of deformity of the angle of the feet, including club foot and flat feet (Schinzel 1991; Horneff 1993, U).

Families say …

" *N does not like to be handled, likes to lie down and roll from side to side, and is very defensive when being touched* - N, age 6.

" *Kerstin is a satisfied, friendly child, very happy in her own small world. It sometimes seems to us as if she has never left the womb* - Kerstin, age 13.

" *Joshua is a mixture of a 7 year old child and a 16 year old teenager. He has difficulty relating to his peers and has always related better to older teenagers* - Joshua, age 16.

" *Monique is happy, placid, willing, friendly and likes being groomed and dressing up. Her spare time activities include swinging, sofa time with mother and long baths* - Monique, age 24.

What about hearing?

You may notice even before diagnosis that your baby does not respond to sound. Most children with PKS known to *Unique* have a marked sensorineural (permanent) hearing loss that requires correction with hearing aids and reports of adults in the medical literature usually also mention hearing loss. However, the precise cause of the hearing loss is not yet understood. In younger children the severity can be difficult to assess but in children whose hearing has been measured it has often been moderate to severe and is occasionally profound. In at least one child, the severity improved with maturity but no child has been shown to outgrow it completely. Children with high palates and clefts are vulnerable to conductive hearing loss caused by glue ear and some children with PKS will be helped by grommets or longer term T-tubes to improve the function of the ear drum (Horneff 1993; Schuster 2002).

What about vision?

You may notice that your baby's eyes do not focus and may appear to search a lot. Many children have a visual impairment. In some the effect is minor, including astigmatism (a defect that results in a distorted image) and disordered depth perception, making it hard to identify steps and other changes of level. Other children have cortical visual impairment (a condition in which the visual systems in the brain do not understand or interpret what the eyes see) and defects in the ability to focus the eyes properly are common. Many children have the rapid involuntary eye movements termed nystagmus and some also have a squint (strabismus) (Mathieu 1997;U).

Will PKS affect a child's behaviour?

Most babies and children with PKS known to *Unique* are placid and tend not to take the initiative and interact with their environment. Although some children are sociable, others prefer to be left alone and some dislike being handled and avoid being touched. In general, they behave like children younger than themselves. Any behaviour problems tend to arise in older children and appear to be more common in those with more extensive communicative and cognitive abilities.

What is known about growing up with PKS?

There is very limited information available on puberty in children with PKS. The information that exists suggests that in some children it may proceed normally or be somewhat delayed and full secondary sexual characteristics (such as body hair) may not develop. Girls who find periods difficult to cope with may be given lomg-term contraceptive injections or implants to control them.

Will a child ever be able to live independently?

Many children with PKS remain dependent on their carers for all aspects of personal care but this is not true of all. Those who are less severely affected may become toilet trained during the day time before school age and at night before they reach secondary school age. They learn to brush their teeth (an electric toothbrush helps) and hair, to dress and to wash themselves. However, only those children who are so mildly affected by tetrasomy 12p mosaicism that they cannot be truly said to have PKS achieve a level of life skills that will allow them to live independently.

What about food and eating?

The experience of *Unique* shows that feeding problems are variable. Many PKS babies have successfully breastfed for months although some needed a period of nasogastric tube or bottle feeding of expressed breast milk. Babies with a cleft or a very high arched palate (described in two thirds of the *Unique* series) have faced particular difficulties and in *Unique*'s experience they have fed more successfully from a Haberman feeder, a feeder for babies with sucking difficulties. The underlying low muscle tone makes feeding a particular effort for most PKS babies and while some feed adequately, they may still lose weight and need supplementation with a high energy formula. A minority of babies have reflux, where feeds readily return up the food pipe from the stomach. In most cases this has been controlled with medication and feed thickeners as well as careful positioning. If these steps do not control

Families say …

" *Monique left school at 21. She was trained at school to wipe books in a public library. She lives now in a specialised family home with another girl and is very active with the family, her friend and with animals.*

" *We video tape programmes of Monique performing tasks, showing her skills, out in the community shopping, and doing her physiotherapy. The videos are then used for staff and everyone else involved in her teaching. There is thus little chance of regression due to people not understanding her programmes or her signing. New staff learn more quickly and are more efficient and helpful* - Monique, age 24.

reflux, it is possible to tighten the valve between the stomach and the food pipe with a surgical operation known as a fundoplication.

A high proportion of babies have little sucking action and may need spoon feeding at first, while some have benefited from a gastrostomy, a tube inserted into the stomach via the body wall to allow all feeds and medicines to be taken directly.

Once babies move on to solids, they typically need mashed or pureed food for longer than other children. While some children remain unable to chew and continue to need their food finely chopped, others progress to family foods by mid childhood.

Any sleep disorders?

Sleep disorders are not a specific feature of PKS and many families describe sleep disruption that is no different in type to any other young child. However, three *Unique* families have reported a continuation of the newborn sleeping pattern with their child unable to distinguish day from night and many families record that their babies sleep for very long hours until a much greater age than other children. Once children learn to sit up and relate to their surroundings the great need for sleep appears to abate. In the meantime, very short therapy sessions may need to be scheduled in order to sustain a child's wakefulness.

What is the medical outlook?

Babies with PKS are vulnerable as newborns. They may be born prematurely and have a raised rate of central nervous system anomalies and apnoeic spells when they stop breathing. They are also prone to respiratory difficulties.

Of *Unique*'s 32 members, two who died as young children had a progressive atrophy of the brain. The oldest patient described in the medical literature was 45 years old and *Unique* has members in their twenties and thirties.

One of the most severe effects of PKS is a diaphragmatic hernia and some babies do not cope with life outside the womb or withstand the very demanding surgery. However, it is not true that all babies with PKS and a diaphragmatic hernia have a poor outlook. Look on the PK Syndrome support group's website at www.pk-syndrome.org for the story of Margaret Wilson (U; Schuster 2002).

Does it help to know the mosaic proportions?

The karyotype (chromosome description) shows the proportion of cells with the additional chromosome. The additional isochromosome 12p is found in specific tissues of the body, particularly the skin and also the lungs, ovaries and testes. However, the proportion in a single tissue sample, of skin for instance, does not necessarily reflect the make-up of the whole body.

What is known is that severely affected children can have very low levels of abnormal cells and in occasional cases no abnormal cells at all have been detected in either blood, amniotic fluid or skin cells. By contrast, a skin biopsy from a child so mildly affected that she did not have true PKS showed a ratio of 4:3 abnormal cells (Schinzel 1991; Bielanska 1996; Doray 2002; Genevieve 2003).

Causes

Children from all parts of the world and from all types of background have Pallister-Killian syndrome. No environmental, dietary or lifestyle factors are known to cause it. So there is nothing you did before you were pregnant or during pregnancy that caused PKS to occur and also there is nothing you could have done to prevent it.

In the process that leads to the formation of the egg and sperm cells, chromosomes usually separate so that each cell receives 23 single chromosomes. A fairly common error is a failure of this natural separation (non-disjunction), so that the cell contains an extra chromosome 12. The 12p isochromosome is then created when one chromosome 12 splits horizontally at the centromere instead of the usual vertical divide. The two copies of the long arm are lost. Mosaicism arises soon after conception when the isochromosome is lost from one cell line. The alternative scenario is that the additional chromosome has arisen from a mistake in cell division after conception (Turleau 1996; Dutly 1998; Struthers 1999; Dufke 2001).

An isochromosome of the end of 12p to p12.3

The additional chromosome almost always consists of the entire short arm. However, one child with typical PKS has been described who had an isochromosome made up of the end of 12p to p12.3, showing that the critical region causing PKS must lie in this segment (Dufke 2001).

The additional chromosome 12 usually comes from the mother but can sometimes come from the father. This type of chromosome mistake is more common among older parents and among *Unique* members many were older. Mothers' ages ranged from 29 to 42 while fathers' ages ranged from 28 to 50.

Can it happen again?

PKS has only been known to occur sporadically, so that the affected couple and other family members appear to be no more likely to have another child with PKS than anyone else in the population. However, there is a very small theoretical possibility that one parent's ovaries or testes contain a proportion of cells with the additional 12p chromosome. This would increase the chances of a recurrence and is the reason you may be offered prenatal testing in your next pregnancy if you wish for it. Anyone with tetrasomy who is thinking about having children should also have a talk first with a genetic counselling service (Doray 2002).

Support and Information

Rare Chromosome Disorder Support Group,
PO Box 2189,
Caterham,
Surrey CR3 5GN,
UK
Tel/Fax: **+44(0)1883 330766**
info@rarechromo.org
www.rarechromo.org

There are two online Pallister-Killian websites, each set up by the parents of an affected child.

Pallister-Killian Syndrome (**www.pk-syndrome.org**) was set up by the father of Filippo Colasanti and is in Italian and English.

PKS Support Online (**www.pksonline.org**) is a group set up in 2003 by two mothers hoping to publish a book on the syndrome.

There is also a lively email support group at
http://groups.yahoo.com/group/pks_support/

Unique mentions other organisations' message boards and websites to help families looking for information. This does not imply that we endorse their content or have any responsibility for it.

This leaflet is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. The information is believed to be the best available at the time of publication and has been verified by Dr Michel Vekemans, Department of Genetics, Hopital Necker Enfants Malades, Paris, France 2004 and by *Unique*'s chief medical adviser 2005