

## **Recommended Clinical Evaluations for the Child with PKS**

While being told that your child has Pallister-Killian syndrome (PKS) can be overwhelming, the benefit of obtaining a specific diagnosis is that it allows for a targeted understanding of many clinical and developmental issues that need to be addressed in a diagnosis-specific manner. Knowing issues that other individuals with PKS have faced in the past has enabled clinicians to develop a series of clinical tests that are aimed at either ruling out specific problems or catching them early while they are easier to manage and treat. Treating medical problems early is not only beneficial to your child's health but will also optimize his or her developmental outcomes. A child in discomfort or with a visual or hearing impairment that is undiagnosed will not be able to develop at their optimal level. Given the rarity of PKS, there are likely several clinical issues that we as clinicians have yet to fully appreciate and we therefore are very reliant on families to educate us and their clinicians at the same time that they are benefiting from their doctor's expertise. The following is a list of targeted exams that we would recommend for any child with PKS. As we learn more and more about PKS this list will evolve and your feedback as parents is critical in this process.

This is a long list of clinical issues and is meant to encompass the medical issues that kids with PKS, as a group, face. Many of these will never be an issue for your particular child and most kids with PKS will only have a couple of these issues to manage.

### **1) Cardiology (heart)**

Approximately 25% of children with PKS will have a congenital heart difference. Sometimes these can be detected by simply listening to the heart to see if there is a murmur (note: while a murmur may indicate a congenital heart difference many murmurs can be normal or "benign"), but some heart differences (such as atrial septal defects (ASDs) which are not uncommon in PKS) do not cause a murmur and can cause significant problems to the child. For this reason we recommend that all children with PKS be evaluated by a cardiologist as early as possible and have an echocardiogram performed whether there is a murmur or not. If the heart is normal then the child is cleared, as a congenital heart defect will be present at birth and not develop later on.

We do recommend periodic cardiac evaluations for all children with PKS (once every year or two, or as recommended by their cardiologist) even for those who do not have a congenital heart difference, as changes in the heart muscle called hypertrophic cardiomyopathy (HCM) have been reported. This is rare but should be checked for at regular intervals.

### **2) Gastroenterology (stomach and intestines)**

Individuals with PKS may have both functional and structural differences of their gastrointestinal (GI) system. The most common functional difference is gastroesophageal reflux disease (GERD). GERD usually manifests as “spitting up” but sometimes the refluxing stomach contents are not actually “spit up” but do cause discomfort in the esophagus (the tube between the mouth and the stomach) which may result in arching of the back or irritability. Some reflux may even be “silent” (without any clinical signs in your child). This should be evaluated for in all newborns and young children with PKS and may involve studies called a milk scan or pH probe. This is an important evaluation because if left untreated this can result in damage to the esophagus due to the acid from the stomach, which if left untreated for many years can result in cancer. Depending on the severity of the reflux some children may need surgical correction of the connection between the stomach and the esophagus, while others will do fine on anti-reflux medicines.

All kids with PKS should also be evaluated in the newborn period for structural differences in the GI tract. The most concerning is intestinal malrotation, where the small intestines are looped in the abdomen in a reverse manner. Children with this finding are at increased risk for the intestine to become twisted (“volvulus”) and if left untreated can rupture, which can be a life-threatening event. This is especially important to identify early as many kids with PKS are unable to vocalize where their pain and discomfort lies and may make diagnosis of a volvulus difficult in an emergent situation with physicians that are unfamiliar with PKS. A simple test called an “upper GI with small bowel follow-through” which is basically a series of X-rays following the passage of a liquid that can be visualized on the x-rays that the child drinks or has placed in the feeding tube, can easily rule a malrotation in or out. This is a one time test as a malrotation is either present at birth or not.

Other GI issues that should be evaluated for in the newborn period include diaphragmatic, umbilical and inguinal hernias, and differences in the anus like narrowing of the opening (anal stenosis) or complete closure of the opening (anal atresia or imperforate anus).

The gastroenterologists and nutritionists are also excellent resources for feeding issues and concerns about growth and weight gain.

### 3) Orthopedics (bones and joints)

While some orthopedic problems are readily apparent at birth, such as extra fingers or toes, there are a few potential problems that will need the targeted attention of an orthopedist. Because of their low muscle tone and lax joints, all children with PKS should be evaluated for congenital hip dislocations. This can usually be easily done with an ultrasound of the hips. Early diagnosis and correction is important and will save later complications and difficulties for ambulation. Another fairly common issue, again likely related to the low muscle tone in PKS, is kyphoscoliosis (curvature of the spine). This usually develops as a later complication but kids with PKS should be monitored regularly for this both by physical exam and radiologic studies if indicated.

#### 4) Ophthalmology (eyes)

While children with PKS can have the same ophthalmologic differences as children without PKS, identifying any visual differences early and treating it will help in optimizing learning and should be undertaken early and on a regular basis. In addition to general visual issues, kids with PKS may be at increased risk for ptosis (droopy eyelids) that may need to be surgically corrected in order to be sure that the child's visual fields aren't obstructed.

#### 5) Otolaryngology/ENT (ears, nose, and throat)

A good ENT evaluation is warranted as there are increased rates of various differences involving the mouth and palate that should be evaluated. Children with PKS have a higher rate of cleft palate (incomplete closure of the roof of the mouth), which may be easily seen on exam or be very subtle and only involve the muscle that can't be easily visualized (called velopharyngeal incompetence). Untreated clefts can result in feeding difficulties, infections and delays in development of speech. Individuals with PKS may also be at increased risk of enlargement of the tonsils and adenoid glands as well as enlargement of the tongue that may result in obstruction of the airway.

There may be structural differences of the ear as well as hearing loss (see "Audiology" below), which may need to be managed by an ENT.

#### 6) Audiology (hearing)

Although the exact prevalence of hearing loss in PKS is not known (as high as 90% of kids has been reported), it is a significant issue and it is recommended that all newborns with PKS have a thorough audiologic evaluation. This should be retested at regular intervals depending on the presence and severity of hearing loss in the child, and should be done by an audiologist and not simply in the pediatrician's office. Early recognition of a hearing loss and appropriate interventions will help to optimize developmental outcomes.

#### 7) Urologist (kidney, bladder, genitalia)

Children with PKS can have a variety of kidney and bladder differences. All newborns with PKS should have a renal (another word for kidney) and bladder ultrasound to rule out any structural differences. Any child with PKS who has had a urinary tract infection should have a functional study called a vesicoureterogram (VCUG) to rule out reflux between the bladder and the ureters (the tubes that drain the urine from the kidney into the bladder).

Boys with PKS are at increased risk of having genital differences such as undescended testes, hypospadias (where the opening in the penis (urethra) is not at the tip of the penis) and other differences. These often need surgical

correction and should be evaluated by the urologist early in the newborn period.

#### 8) Dentistry (teeth)

Although tooth eruption may be delayed, most of the dental issues faced by kids with PKS are the same as other children. Sometimes treatment can be complicated by developmental delays and it may be necessary to do exams and procedures under general anesthesia. For this reason it is best to develop a relationship with a pediatric dentist who has experience with special needs children and to try and be seen by 1 year of age.

#### 9) Developmental pediatrics

One of the major, and most challenging, issues that parents have to deal with is that of cognitive delays in their child. While there are no specific treatments targeted at kids with PKS for these issues, having annual visits with a pediatric developmental specialist has many benefits. These evaluations will help identify those areas that may need more, or less, focused therapies and help develop an individualized therapy plan for your child. The developmental pediatrician is also a valuable advocate for implementing appropriate programs in your child's school.

#### 10) Neurologist

Most families with a child with PKS end up seeing a neurologist at some point, often early on due to the low muscle tone (hypotonia). Low muscle tone is almost universally present in children with PKS but may evolve as they get older into increased muscle tone (hypertonia). This can result in contractures (tightening of joints) that may need surgical treatment if left to advance. The neurologist can monitor this and recommend targeted physical therapy to help keep these joints loose.

Seizures are another major concern for families with a child with PKS. Up to 80% of children with PKS will develop seizures at some point. These can be severe and if undiagnosed or untreated can have a devastating impact on the child's growth and development. Early diagnosis and management is critical, although some children's seizures are quite refractory to treatment. An early and close relationship with a good pediatric neurologist is essential.

#### 11) Genetics

Most geneticists are familiar with PKS and may serve as a good resource to coordinate care and management of your child's medical and developmental needs. While some pediatricians are comfortable with children with multiple needs, often times your pediatrician will serve as a resource for general pediatric care (i.e. immunizations, treating common pediatric illnesses like ear

infections, diarrhea etc...) and the geneticist will make sure all PKS specific care is being undertaken at an appropriate time.