COSTELLO SYNDROME

A BOOKLET BY PARENTS FOR PARENTS

Welcome!

We hope to provide you with support and understanding, and share what we know as we learn more about this very rare syndrome. If you are interested in looking at more photos of our children, they are available at http://costellokids.com/.

Costello syndrome *is a rare RASopathy resulting from germline mutations of the proto-oncogene HRAS. Its phenotype includes severe failure-to-thrive, cardiac abnormalities, a predisposition to benign and malignant tumors, hypotonia, and developmental delay. [-- Axelrad ME, et al, AJMG, 2011]*

A detailed review on the management of Costello syndrome can be found here:
http://www.ncbi.nlm.nih.gov/books/NBK1507/

A deeper explanation of the genetics in lay terms can be found here:
http://ghr.nlm.nih.gov/condition/costello-syndrome

By now, you have probably gone through an unusual pregnancy with polyhydramnios, your baby was large for gestational age, and possibly premature. Hang in there! The road is rough, but Costello syndrome's list of features includes a "friendly, sociable, engaging personality," which our families cherish.

GENETICS

Costello syndrome (CS) is the rarest of the RASopathies, affecting about 300 people worldwide. Unlike the other RASopathies, the only mutation that causes Costello syndrome is HRAS.

TESTING

If you have not yet had your child tested for the HRAS mutations, we strongly recommend that you do! One reason is because for some, it's hard to tell if the child has Costello syndrome or one

of the other "RASopathies", and while they share some issues, there are issues that are unique to each syndrome. For example, children with Costello syndrome have the highest risk of cancer among the RASopathies. Testing will also help researchers looking for clues about how the different mutations on the HRAS gene work.

In the United States, insurance companies usually approve a doctor's request for the test, and in most states, Medicaid will pay for it too. A list of clinical laboratories that test for CS can be found at http://www.ncbi.nlm.nih.gov/gtr/tests/?term=C0587248%5BDISCUI%5D&condition=C0587248&compare_labs=1/.

In the UK and Europe please discuss genetic testing with your doctor who will make arrangements for the testing to be carried out.

Because our children's syndrome is so extremely rare, it would be unusual for people to consider Costello syndrome prenatally if it was the first child, but there are labs that will test prenatally.

If you have not had genetic counseling, we urge you to ask your child's doctor for this service. Your having a child with a rare genetic condition makes you eligible for this service. Next are basic questions about Costello syndrome that should be raised in a genetics counseling appointment:

All the CS doctors and researchers who attend the international meetings on genetic syndromes of the Ras/MAPK pathway (of which Costello is one) agree that the only mutations that cause Costello syndrome are those on the HRAS gene.

If your child tests negative for HRAS, your child does not have Costello syndrome. ***But*** please rest assured our family organizations will not turn you away. While you will notice that the issues described in this booklet don't quite fit well for your family's needs, you can contact Lisa Schoyer at lisa@rasopathies.org for additional information and support.

Q: What are my chances of having another child with Costello syndrome?

A: Your chances of having another child are low. On our listserv of more than 125 families, only one family had another child with Costello syndrome. Researchers know that Costello syndrome is **autosomal dominant**, meaning that it affects one of the two copies of the HRAS gene mutation (on chromosome 11) and it only takes one copy to have the mutation to cause the syndrome. This can happen a few ways, from the most common to the least:

1. The mutation occurred in the egg or sperm cell, or just after fertilization (also known as new or **de novo** or **spontaneous mutation**), which explains why a genetic disorder affects every cell but there is no family history of CS. Spontaneous mutations in general are not uncommon, and do not survive past the first few weeks of conception.

   This is the most likely way that your child developed Costello syndrome. The most common mutation appears to have come from the sperm. Though the father doesn't have the syndrome, the sperm is constantly being made. So as he grows older, the risk of a "copying error" in the sperm increases. For CS the copying error is on the HRAS gene.

2. One of the parents has the mutation in *SOME* of his or her cells, as the result of a *partial* spontaneous mutation in the parent (a grandparent's egg or sperm). This is called **mosaicism**, and is very rare, even for Costello syndrome! The most effective way to for geneticists consider this kind of mutation transmission is if there are siblings with Costello syndrome in the family – learning from the siblings, rather than being able to test for it. Otherwise it's by luck. In one super-rare case of CS, mosaicism was found because the CS mutation was in the parent's cheek cells for the preliminary gene test – but not in the blood cells for the confirmatory gene test!

   There are very few known sets of siblings with Costello syndrome, mostly reported in articles published before the gene find in 2005. Two sisters in Norway who were originally both diagnosed with CS before 2005 were tested after the gene responsible for CS was identified. One turned out to have Costello syndrome (HRAS mutation), and the other has a KRAS mutation (associated with Noonan and CFC syndrome). Another set of siblings clinically diagnosed before 2005 were confirmed to both have the HRAS mutation.

3. The child inherits a mutation from one parent – who also has the syndrome. There are no known children who have inherited Costello syndrome this way. Looking forward, this means that if your child with Costello syndrome has children, your grandchild has a 50% chance of having Costello syndrome.

Q: How does this affect my healthy children?

A: Your healthy children are not affected at all by Costello syndrome. The only way your healthy children or their children could have a child with Costello syndrome would be if situation (1) or (2) listed in the previous answer were to happen, the same chance as anyone else. With what we guess to be about 300-500 cases identified worldwide, our children **are** the information from which the scientists and doctors are making theories! If we use the numbers known in the United Kingdom to generalize, the prevalence is 1:300,000. Japanese researchers sent out a survey across the country and the results from those who answered the survey, which they published is 1:1.25 million.

The Importance of Parent-to-Parent Communication

In addition to doctors and researchers observing our children for patterns, we parents are active and determined to develop a more detailed picture of what Costello syndrome is. Our direct communication with each other can speed up the identification of a pattern, and starts an immediate database for a doctor interested in following the research.

Here are some shared observations many parents notice but are still mysteries:

- Our children are "hot-blooded." Whether it's the metabolism or the heart issue (both can cause a person to be hot all the time) or something else, or all of the above, many of our children **sweat a lot** - even to be a bit "ripe-smelling" like adult body odor.
- Some children, especially when they're very young, experience **unexplainable fevers**. This could be due to their neurological systems not being able to regulate their body temperatures very well, rather than being the result of an infection – but an infection must be ruled out first.
- Many parents notice their child is very **sensitive to sunlight** as well as **touch**, particularly the hands and feet.
- Most parents talk about difficulty **sleeping** through the night that starts in the early years with a lot of crying that sounds like it's from pain, waking up many times in a night, waking in a pool of sweat requiring sheet changes, startling, sleep apnea (CNS and obstructive), and can include teeth grinding. Some children are diagnosed with sleep terrors. Some grow out of the very light sleeping, but many don't.
- A number of parents shared stories about excess **earwax** which required regular visits to the doctor to remove. Ear canals varied in size, but those whose ear canals were narrow also talked about them being 'not very straight'. Families also talked about how itchy their children's ears are too.

THE GASTROINTESTINAL SYSTEM

We are still looking for a gastroenterology researcher!

This system is just about always involved, and some kind of intervention is needed. **This is the most chronically difficult issue for our families.** The vomiting and the sleepless nights from the vomiting/pain are among the hardest problems to live with. Many things probably contribute to this, from low muscle tone (**hypotonia**) that can affect the mouth which affects lip control, tongue coordination, and peristalsis through the gut (which is one long smooth muscle - the type of muscle most affected by low muscle tone), a high arched palate, poor suck-swallow coordination, and possible tracheomalacia, laryngomalacia, or tracheolaryngomalacia (floppy/redundant tissue in the throat that usually resolves by about 4 yrs old), acid reflux, slow emptying of the stomach, and possible inefficient absorption of nutrition (documented in a few children).

Families of older children outside the USA and Canada share early childhood stories where they spent time in the hospital every couple of months or so, with ng- (nasogastric) tube feedings and IVs for dehydration, or feeding their children via ng-tube at home.

Over 90% of our children need medical intervention for nutrition, either through a nasogastric tube (**ng-tube**), or gastrostomy tube (**g-tube**), which go directly through the stomach wall for feeding. US and Canadian doctors tend to choose g-tubes when a child is very young, while doctors from other countries will have an ng-tube for a while before a g-tube is considered, sometimes a year or more.

Nutrition is provided by "bolus" (pouring in the formula or meal in one sitting) or timed drip-feeding (requiring a pump, sometimes starting with round-the-clock feeding if the rate of feeding tolerated is so slow that's what's needed). Some children get a surgical procedure, a Nissen fundoplication (**fundo**), where a surgeon wraps the upper stomach around the lower end of the esophagus and stitches it in place to prevent gastric acid to reflux into the esophagus. But for some children, the "fundo" is not appropriate. A small number of children have g-j tubes (gastrostomy-jejunostomy tubes), which go through the abdominal wall into the jejunum, the part of the small intestine closest to the stomach. One child's GI tract is so compromised that she relies on TPN (total parenteral nutrition, through a central catheter line into a major vein).

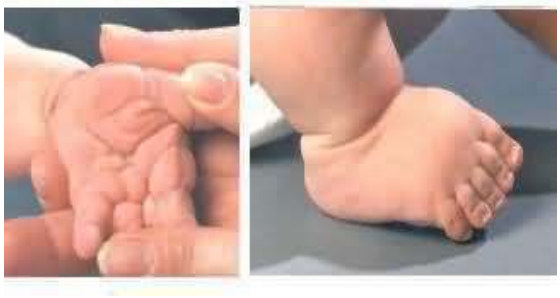
The **rate of feeding** has been a serious issue for many families whose child has a g-tube or ng-tube. Some need to start slower than 60cc/hr. One parent had to start at 5cc/hour. These children also have a hard time returning to their usual g-tube flow rate after "NPO" (nothing by mouth) for procedures like surgery. Keep an eye on this and document it because you may need to provide evidence so your child's doctor has evidence to slow the flow rate to

meet your child's need. The balance is in providing nutrition at the maximum tolerated rate, to build your child's reserves.

Even with medical intervention, many of our parents report that their children vomit a lot in the early years. For children who are transitioning out of this stage (seldom or even not vomiting anymore), parents have reported the slightest issue like a common cold causing the vomiting to start again. Our children's guts are very sensitive.

Good news, **the feeding and vomiting issues usually resolve themselves** anywhere between the ages of 2 and 12 years old, with most resolving closer to the 2 to 4 year-old end of the age range. There are a few cases where the child will clearly need the g-tube for life. There are also a few children that had mild feeding issues that they never needed a g-tube.

Many children have difficulty with diarrhea in the very early years, but as they grow or with certain (or a combination) of meds treating other issues, **constipation** can be a problem. All do better with more fluids, but it's hard to get a child – any child – to drink enough. For children with an ng-tube, a g-tube or a g-j tube, this is less of a problem. The "Mush-Push" strategy (Howard A. Heit, MD, in Leavitt 2004) might be worth talking to your child's doctor about, to see if it makes sense in your child's case. "Mush" is a stool softener, with "push", which is a mild bowel stimulant.



More families are finding success in blenderizing foods to bolus feed their children when beyond the breast milk diet phase. Vomiting is often reduced or eliminated with a blenderized diet. Parents noticed their children are more interested in eating orally once they have had real food through their tube. You can contact Angel, mom of Westin at angel@costellosyndromeusa.org for information and support.

ENDOCRINE SYSTEM

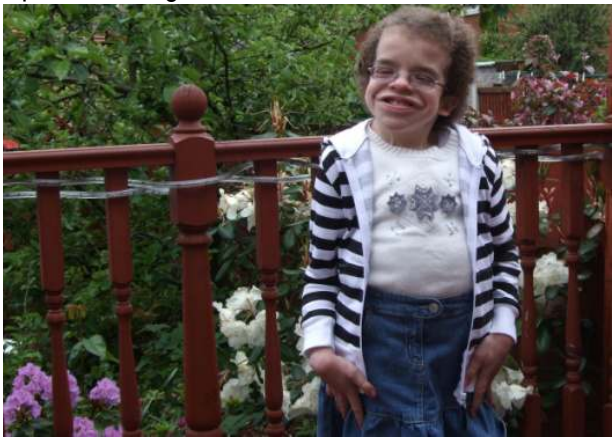
All our children will be short, this is something that all RASopathies share. Growth hormone treatment is controversial to increase height alone because of the risk of cancer and HCM (hypertrophic cardiomyopathy), both which develop because the cells are instructed to grow beyond what's healthy.

Nevertheless, an unusually high number of our children have growth hormone deficiency (Dr. Doyle identifies about half the teens he studied). Treatment with growth hormone therapy (GHT) is something for the family and the child's doctor to talk about, weighing risks and benefits.

Perinatal (from just before to just after birth) hypoglycemia has been documented about CS. Hypoglycemia can also be a clue to growth hormone deficiency if a child is beyond the perinatal stage.

ORTHOPEDICS

Our children's **hands**, **ribs**, **arms**, **ankles**, **hips** and **spine and spinal cord** are involved.



A number of our children's **hands** are fisted in very early childhood. Finding small objects that they can't choke on are a good way to spread the hand open. They may need "splints" (braces hand-made of neoprene material to help keep the hand open. Two moms on the listserv talked about how stinky the fisted hands were, from lack of air circulation.

Most children's hands (and feet) have lots of loose skin (cutis laxa), are ***very*** flexible, and tend to turn away from the midline ("ulnar deviation" – towards the ulna bone in the forearm). The hyper-flexibility makes it hard for fine motor strength in their hands.

The appearance of our children's hands look to be the one clear factor that separates Costello syndrome from Noonan or cardiofaciocutaneous (CFC) syndromes.

Several parents report their child has **vertical talus**, which can be corrected with medical intervention. Depending on the severity and situation, casting (putting a cast on the feet) may be tried before surgery.

The **ribs** are typically unusually shaped, which may explain why many don't go through a crawling phase, even with therapeutic intervention.

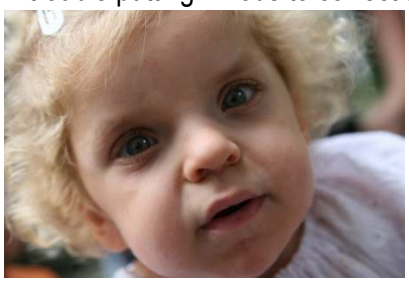
Rolling, sitting and walking will be delayed. Several children have wheelchairs to help them get around school, which over time have been replaced with walkers. (They have little protection reflex if they fall.) While his protection reflex isn't the greatest, one boy loves to play basketball and ski -- unassisted!

Because of the low muscle tone and plantar flexion (toes pointing down – though there are a couple of children who have dorsiflexion – foot pointing upwards) many children find support with ankle-foot orthotics (AFOs or DAFOs or SMOs), and have their Achilles tendons casted (to stretch the tendons) or "released" surgically. Several children have also gotten hip tenotomies (hip tendon-releasing surgery), with generally good success. A few have had hip reconstruction surgery.

Most children have trouble straightening out their **elbows**. Australians call them "kangaroo arms."

Our children have **low muscle tone** (hypotonia), which might be confusing because of the tight tendons which cause joint contractures.

Several children develop **scoliosis** (the spine curves sideways) and have braces for their backs. Some have had surgery. There are a few children whose bones are so soft that they cause complications. One child's doctors had trouble putting in rods to correct the scoliosis because the bones were so soft, but the chemotherapy for her cancer may have contributed to softening the bones. **Kyphosis** (the spine curves outward) is not unusual either, but the thought among orthopedists these days is to leave it alone, as the cure is worse than the problem. And many of our children have the two – kyphoscoliosis.



NEUROLOGY/NEUROSURGEON'S EXPERTISE

A few parents have reported their children have tethered spinal cords, and a few ***develop*** syringomyelia and **Chiari 1 malformations** (this is unusual!). Some need to be surgically repaired. Dr. Karen Gripp's publication, ***High incidence of progressive postnatal cerebellar enlargement in costello syndrome,*** can help your child's neurologist or neurosurgeon determine how to monitor this.

Several families whose children had **tethered spinal cords** released surgically reported retethering to the spinal cord.

THERAPIES and Developmental Support

Our children do very well with **Occupational, Speech** and **Physical Therapy** (**OT, ST** and **PT**) and **developmental support services.** For the very young children (infants as young as a month old), an OT may be authorized by the

insurance payor to provide all three therapy services. Especially for very young children who need these therapies, it's important to find someone with a lot of experience.

In the US, services including developmental services, supports, therapies, assistive technology, and special education can be provided under the federal Individuals with Disabilities Education Act (IDEA). Services for children from birth through age three are covered under the Part C of IDEA. Then special education (IDEA Part B) services are mandated for children from ages 3-12. IDEA and Section 504 of the Americans with Disabilities Act (ADA), provide a number of rights and protections. Two good resources to learn more can be found at Wrightslaw http://www.wrightslaw.com/ and the Center for Parent Information and Resources http://www.parentcenterhub.org/.

Speech therapy (**ST**) is strongly recommended, as the children appear to respond well. ST can be provided by a Speech Language Pathologist (SLP), or an Occupational Therapist (OT). Many children learn sign language and may have assistive technology (**AT**) such as iPads to help them until (or if) their speech develops well enough.

Our children's receptive language skills appear to be much better than their expressive skills. **Speech** is delayed and limited. It's probably connected to the poor oral-motor coordination overall, small mouths and slightly larger-than-typical tongues (macroglossia) and low muscle tone.

Assistive Technology (AT) – In addition to communication, iPads are showing to be a great aid for our children. Many apps are available to help them build their skills. For more resources on assistive technology, look at the Family Center on Technology and Disabilities: http://www.fctd.info/

VISION

A higher-than-average number of children have **myopia** (near-sightedness), often with **lateral-beating nystagmus** (the eyes jiggle – horizontally), and some have **strabismus** (cross-eyes). Except for some children having delayed vision (several parents talked about being fooled by their child's effective use of hearing to mask their visual delay!), most visual issues appear to be correctible with glasses.

Many children have a hard time walking down stairs or stepping across different-patterned floors, because they have difficulty interpreting the lower "quadrants" of their field of vision. Some parents report that their children responded well to **vision therapy**.

HEART

Most of our children have heart issues, but this can be anything from mild arrhythmia to such severe HCM (hypertrophic cardiomyopathy) that the child dies from it (not common). Because of this, it is recommended that your child get an **ultrasound** and an **echocardiogram** to see if there are any problems. An article by Angela Lin, M.D. and associates, ***Clinical, pathological and molecular analyses of cardiovascular abnormalities in Costello syndrome: A Ras/MAPK pathway syndrome,*** published in the American Journal of Medical Genetics in 2011, will give your doctor medical justification for this test. Dr. Lin recommends, at the least, a baseline echocardiogram (EKG or ECG).

CANCER

The most common cancer is rhabdomyosarcoma (RMS); and a few children have developed neuroblastoma tumors. Older children have developed bladder cancer. Bladder cancer typically develops in people over 60 years old, but has been seen in teens with CS. Fortunately, no one with CS has died from bladder cancer.
The current estimate for risk for any malignant tumor (cancer) is about 15%.

Lisa Schoyer (a mom) is very interested in collecting information about this, so if your child does develop RMS, please contact her. She would appreciate all the data that can be gathered, in order to be as accurate as possible. (See back panel.)

We urge you not to worry about cancer before thorough testing has been completed (confirmatory testing after a positive screening test - this may include a tissue sample, nuclear imaging and other more intense tests), because there is a chance that it may not be cancer.

Karen Gripp, M.D. and associates' 2002 article, ***Five additional Costello syndrome patients with rhabdomyosarcoma: proposal for a tumor screening protocol***, in the American Journal of Medical Genetics is a good resource, but an important lesson was learned after its publication. The neuroblastoma screening (using a urine sample), turns out to produce more false positives than actual positives, so they could make us worry needlessly. In a 2004 follow-up article, Dr. Gripp recommends not using this screening method because of the false-positives -- ***Elevated catecholamine metabolites in patients with Costello syndrome***.

Cancer Screening – Dr. Gripp's publications recommends abdominal and pelvic ultrasound screening for rhabdomyosarcoma and neuroblastoma every 3-6 months until age 8-10 years old. She also recommends an annual urine test for hematuria, a screening test for bladder cancer, starting at age 10. But since those publications, it doesn't appear that the screening protocol has made a difference in the outcome of our children who did develop cancer.

In addition to Dr. Gripp's recommendations based on studying over 15 children with CS, a 2010 article by Dr. Ahmadi, an otolaryngologist recommends nasal endoscopy examinations every 4-6 months and MRIs of the head and neck less often - after reporting on one (1) child with a tumor in that area of the body. That child's tumor was identified when it was at stage II in the process of ruling out all possibilities, and was successfully treated, without the recommended regular nasal endoscopies.

Several CS specialists question the effectiveness of cancer screenings, citing well-documented studies on women with recurring breast cancer. Those reports confirm strongly that *waiting for the results* is the worst part of their entire experience. We urge you talk to your child's geneticist or genetic counselor to fully understand how the screening process works, and the risks and benefits involved.

THE SKIN

Your child's doctor may talk about **papillomata** – wart-like skin growths, because they are described in the literature. These may start to show on your child starting at age 2, or they may never show up. Doctors recommend testing any skin eruption to distinguish between papillomata, which can be benign tumors, and wart-like "lesions." Some children develop **Acanthosis Nigricans**, the darkening of the skin. Dermatologists' treatments for this appear to work fine, for the most part. **Itchy skin**, from mild to extreme (very frustrating!), and calluses that build up in uncommon places are also common problems.

SEIZURES?

Several children have developed seizures as the result of known causes. But there appear to be increasing numbers of newly diagnosed children with seizures that happen for unknown reasons. At this time, we don't have

enough information to link it to Costello syndrome. With genetic testing, we are finding that some of these children have CFC (cardiofaciocutaneous) syndrome, but not all. This may be something that's showing up in addition to the Costello syndrome effect. One child had seizures that went away when surgery was done on her Chiari malformation (a deformity in the brain where the brain and the spinal cord connect) -- which, before the surgery, wasn't clearly the source of the seizure. If more parents report on this, we will have better information from which to prove or disprove a link!

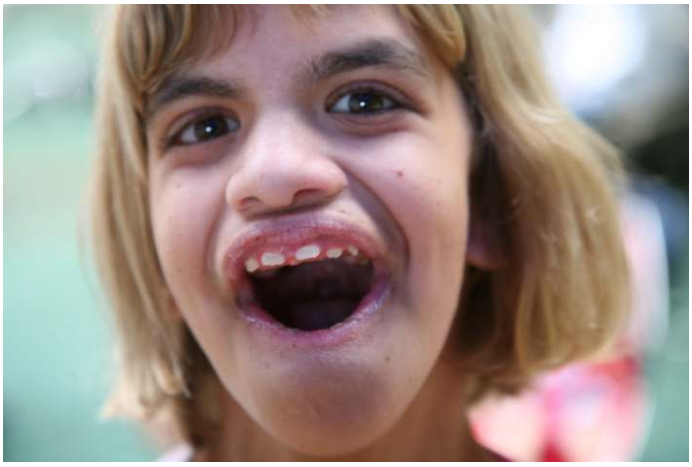
MENTAL AND BEHAVIORAL HEALTH

More parents are reporting that their child experiences increased levels of anxiety, and requiring medical intervention. If your child is showing signs of anxiety, it's worth talking to your child's doctor about it for treatment (therapy and/or medications – families have reported both strategies with success). Others report negative behaviors such as hitting their head or other reactions when they are frustrated. A developmental pediatrician, behaviorist, psychologist or psychiatrist familiar with children with special health care needs may be able to help you if the behavior is distressing to you or your child. Marni Axelrad, PhD, has published a series of reports from studying our children for over 10 years, tracking our children's cognitive, adaptive, and behavioral characteristics. The most current publication, ***Neurocognitive, adaptive, and behavioral functioning of individuals with Costello syndrome: A review***, published in April 2011, may help guide your child's doctor and school on your children's behavioral and cognitive development.

Our children may have "global developmental delays" and intellectual disabilities that will compromise their ability to live independently, but they generally eventually reach all the childhood milestones. Thank goodness for their "**warm, social personalities**" often described in publications! It kicks in usually after the gastrointestinal issues start getting resolved. Many parents report that wherever they go, they endear people to them. And their sense of humor – mature beyond their developmental age – helps us help them through the tough times. Have you noticed?

In addition to the primary pediatrician, a typical child with Costello syndrome may see many doctors, including (but not limited to):

- a geneticist
- a gastroenterologist
- a cardiologist
- an orthopedist
- an endocrinologist
- a neuro-ophthalmologist
- a pulmonologist
- an ENT (ear, nose and throat) specialist
- a pediatric dentist specializing in craniofacial deformities
- a neurologist
- a developmental pediatrician



Our children are amazingly tough survivors.

A FEW OTHER THINGS

Lifespan - We know of a small number of people with CS in their 50's but no real studies have been done. Costello syndrome is so new (gene test just came out in 2005) that it will take a while to collect lifespan data. Most people with Costello syndrome do not live independently as an adult.

Many parents talk about trouble with stuffy and/or runny noses, so that something as minor as a cold can fill a stomach with mucus, causing increased vomiting. Combinations of over-the-counter medications can help some,

but not get rid of the problem. Those who have had **tonsillectomy** and/or **adenoidectomy surgery** do better. Several children who didn't sleep well did better after this surgery – but not all.

Some children also have **tracheomalacia** and/or **laryngomalacia** or both. A small number of children had it severely enough to need a tracheostomy. Fortunately, the ones who do have reported growing out of this. One child who had a trach (**tracheotomy**) grew out of the need for it in a couple of years.

Our children need more calories too.

We've noticed that a good number of our children **metabolize pain medications** very quickly. Be sure that you tell your child's doctors so that pain management and other medications can be carefully observed so as to be more effective.

If your child needs surgery, be sure to ask for the anesthesiologist's help. One parent was alerted by a very observant anesthesiologist, who not only gave a copy of his report to her, proving how her child had needed more **anesthesia**, but he also instructed her to be vigilant with each future anesthesiologist her child sees.

YOU ARE THE EXPERT ON YOUR CHILD

Be prepared to be the one who knows the most about your child, and the key person for your child's medical and educational needs. If you're up to it, ask for copies of all your child's medical reports so that when you visit the next doctor, you have all the information at hand. It makes a **big** difference! *Even if you don't understand them*, being able to provide reports to each specialist helps that specialist immensely! Because of the complexity of multiple issues, your child needs to be seen by the best in each field – if possible.

Some parents have noticed that a specialist who is able to say "I don't know" is someone confident enough to recognize his or her limitations, and that doctor is being honest with you. The odds of their having treated another child with CS are really low. You are building and maintaining a team to support you. You need to be able to trust them with what they do – and don't know.

Your child's care team may need to be reminded that YOU are with your child for life, and the specialists are not. Trust your instincts, and do what you can to educate yourself so that you are taken seriously when you meet with the specialists your child will need to visit.

If you have access to the internet, join our listserv to learn, share and get parent-to-parent support! Here's the web address to go to: http://costellokids.com/webform/join-support-group/

Next Steps: With this new way of thinking about Costello syndrome and the other syndromes on the RAS Pathway, a number of possibilities for treatment can be considered! Cancer researchers and basic scientists already know a lot about this pathway, and are being encouraged to translate their information to our children. It could be that an existing medication could help cure our children of the worst effects! **Incredible** work is being done internationally on our children's syndrome. Members of our Professional Advisory Committee are actively researching and recruiting researchers. Your participation would be greatly appreciated!

In the meantime, treat each of your child's problems based on the specialty of the problem. Remember that your child shares your genes - and has needs and responses like any other child. Not everything can be "blamed" on the syndrome.

While they have incredibly challenging issues, our children are wonderful and amazing sons and daughters.

Please Contact Us!

ICSSG (International Costello Syndrome Support Group)
UK Registered Charity Number 1085605
Colin Stone, Webmaster and Founder, father of Helaina
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United Kingdom

CSFN (Costello Syndrome Family Network)
a 501(c)(3) Non-Profit Organization
Sandra Taylor, President, mother of Jill
info@costellosyndromeusa.org
PO Box 516
Woodinville, WA 98072-0516
(848) 228-CSFN (2736)
www.costellosyndromeusa.org

Join the Support Group and Listserv" at http://costellokids.com/webform/join-support-group

You can also find us under **Costello Syndrome FaceBook**

Another resource:

RASopathies Network USA
a 501(c)(3) Non-Profit Organization
Lisa Schoyer, Chair, mother of Quin Johnson
lisa@rasopathies.org
244 East Taos Road
Altadena CA 91001-3953
USA

RASopathies Network USA is part of **RASopthiesNet** whose mission is to develop a place for families and researchers to learn and share information towards improving outcomes for all families with a RASopathy. The more common syndromes include Costello syndrome (CS), CFC syndrome (CFCS), Neurofibromatosis type 1 (NF1), Noonan syndrome (NS), Noonan syndrome with multiple lentigines (NSML) – also known as LEOPARD syndrome (LS). For more information, go to http://rasopathiesnet.org

Photo credits

Rick Guidotti, http://www.positiveexposure.org/home.html
And the parents of Helaina Stone, Kelsi Moore, Jayne Keizer, and Quin Johnson (in memoriam)

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