What is PTLS?
Duplication of chromosome 17p11.2—also known as the Potocki-Lupski Syndrome (PTLS), or dup 17p syndrome, is a newly recognized condition which can cause a variety of health problems including low muscle tone, poor feeding, heart defects, developmental delay, speech and learning problems, and autism.

What causes PTLS and Why Does It Happen??
Lorraine Potocki, M.D.
James R. Lupski, M.D., Ph.D.
Individuals with the genetic condition designated as dup(17) (p11.2p11.2), or dup17p or PTLS carry extra genetic information on the short arm (the “p” arm) of chromosome 17.

Even though SMS and PTLS are caused by the same genetic mechanism, they are very different clinically. Also, these syndromes have never been reported to occur in the same family. Since the deletion is easier to see on a chromosome study, SMS was recognized before PTLS.

At this time, most persons who have PTLS are diagnosed by a “microarray test” rather than by a chromosome analysis or FISH test (www.bcm.edu/cma/).

This extra piece is actually a duplication of a normal section of the short arm of chromosome 17. This segment contains about 25 genes which are normally present in only 2 copies. An individual with PTLS has 3 copies of those genes. The PTLS duplication usually occurs during the process of meiosis and can happen in either the egg cell or the sperm cell before conception. Simply stated, this duplication happens because we are human—because of the way our human DNA is structured. This duplication can happen in any person’s egg or sperm cells—and if conception occurs, a child is born with dup17p.
A Mother’s Journey
Julie and Christian Smith-Centeno

August 11, 1987 was an incredible day. It was the day an amazing little boy entered into the world after nine months of waiting. Christian was delivered by C-section due to fetal distress. He was too busy studying his new surroundings to worry about crying; this concerned the doctors. Oxygen was given to him until he cried loudly. This little guy didn’t spend much of his young life crying. When he did cry though, it was a demanding one. Christian was very alert and always aware of his surroundings. What got my attention in his early years were his unusual body movements and despite his properly scheduled eating habits, his overly slender frame. His gastroesophageal reflux might have caused a bit of a lower body weight, but not enough to warrant his borderline “failure to thrive.” Christian’s unusual body movements were another story. You would often find him twirling his hands and feet. When sitting in a car seat, he would rub the backside of his feet up and down the seat for the majority of the ride. As Christian began sitting up; he would focus intently at a spot directly in front of him on the floor, lift his legs into the air with them spread into a “V” position, and twirl his hands and feet (picture above.) The odd behavior could be broken by me simply placing my hand over the area where he was focusing. It was amazing to watch. This was something that most doctors brushed off as “babies do all sorts of odd things.” The odd behavior changed into other stemming behaviors as Christian grew up; rocking and twirling, pacing back and forth. He now tells me that he was listening to a “radio” in his head and was, “hopping and skipping to the music.” Christian’s verbal skills were poor, even after he had a velopharyngeal insufficiency repair to correct his nasal emission and poor tone of his tongue. He required speech therapy well into his high school years.

As a nurse with a physical medicine and rehabilitation (PM&R) and pediatrics background, and the niece of the frontier in PM&R and head of the department at UTHSC, Dr. A. Grant, one would think I would have an edge on finding answers, a diagnosis, and an understanding to what this was, by tapping into the many resources I had. To my amazement, no one had an answer. I was given a lot of guesses, but no answers. I was working for a top pediatric group that supported me on my quest. I would sit and rummage through their medical books and discuss various tests that might help. In those days, the only diagnosis given to him was Pervasive Developmental Disorder. According to the neurologist, he could not be truly diagnosed autistic until he was five years old. That was actually a Godsend, now that I look back. With the attention autism is getting these days, he would have been given that label and the quest for an underlying diagnosis may have been dropped. Christian did display all the symptoms one would look for in autism; lack of eye contact, no response when his name was called, lack of interest in toys [very tactile], delayed speech development, etc. My instincts told me it was more. I refused to settle for autism or “unknown.” One day I was reading about Fragile X syndrome. I inquired about genetic testing to rule out this diagnosis.

The Molecular Study

Dr. Lupski has been involved in the clinical and molecular investigations of deletion 17p11.2 (Smith-Magenis Syndrome (SMS)) since 1990. He uncovered the molecular mechanism of this microdeletion syndrome, thus establishing a molecular model for other microdeletion syndromes as well. Dr. Lori Potocki joined Dr. Lupski’s laboratory as a postdoctoral fellow in 1995 to further investigate the clinical features of SMS. In 2000, they established the molecular mechanism for duplication 17p11.2 as the reciprocal product of the SMS microdeletion, and since that time have collaborated on investigations of PTLS. Presently, Dr. Potocki conducts the clinical research study at Texas Children’s Hospital, and Dr. Lupski is the Principal Investigator of the molecular research at Baylor College of Medicine. Patti Robbins-Furman, genetic counselor, joined the team in 2004. Our research coordinator, Dianne Dang joined the team just over a year ago. Together, and in collaboration with several professionals at TCH and BCM we are determined to define both the clinical and molecular characteristics of PTLS!

The Molecular Study

There is no cost for participation in the molecular research study. We request blood samples from the person with PTLS and his
I was blessed to be placed in the hands of a geneticist who happened to be studying deletion 17p, or Smith-Magenis syndrome (SMS) who thought to look closely at chromosome 17. He told me of the duplication and that it was “like looking for the one tree that fell in the forest.” The geneticist knew of only three other individuals in the world with this condition. He however did not know of anyone who was studying it. The doctor told me to check back in a few years to inquire about the status of any possible studies. I called every six months. Christian was four when he was tested, but it was not until he was nine that we were told about the research study at Baylor College of Medicine. We entered the study along with a young man who had SMS. That was the beginning of my quest to help find others with this duplication, and to help educate the medical profession.

Christian graduated from high school and has recently celebrated his twentieth birthday. He works at the local minor league baseball field greeting the community and handing out programs. He continues to display uncontrollable hand posturing (when his mind is focused on something), poor fine motor skills, delays in cognitive development, and decreased reaction time (so he won’t be driving any time soon). He is capable of using the microwave, dressing himself, and caring for himself during the day. He has a strict routine with regard to his eating and sleeping schedule, though this can be disrupted when he is given notice. He has an incredible mind for maps, roads, and geography. Since his academic level is between the 5th and 8th grade, a degree does not seem likely. Christian’s view on life is wonderful and he has chosen to use writing to express his views. The “Christianville Spirit” newsletter goes out to family and friends on a regular basis.

Now that Christian is older, my goal is to be a resource for other families who have a child or adult with PTLS. Because of my background and experience, I can also be a resource for health care providers who care for individuals with PTLS. My request to the medical community is to stop and listen to a parent that says, “Something is not right with my child.” A mother’s instinct goes a long way; a compassionate physician, however, goes even farther.

We have the wonderful ability to make choices in life. With our children, we can choose to get upset, and focus on all of the challenges, or look at it as a blessing that very few people get to have. We are then able to look through the eyes of these children and see the life they live in. It will come with some challenges, some frustrations and yes, many tears. It will also come with joys, laughter and unique situations. As Christian will tell you, “I do not have special needs, and I am not disabled, I am just me…special!”

Christian and I are very happy to talk with any parents that have other questions or curiosities about life with Duplication 17p11.2. You can reach us at 972-208-0964 or email Mapmancc@aol.com or Julie8788@aol.com. Read Christian’s blog at: http://thechristianville.blogspot.com

Thank You, Julie Smith-Centeno

The Clinical Study

The purpose of the clinical protocol at the General Clinical Research Center at Texas Children’s Hospital in Houston is to help determine the medical problems and developmental challenges faced by individuals with PTLS. In addition to being evaluated by several professionals in our team, each participant undergoes a sleep study, echocardiogram and other clinical tests during the protocol. Studies like these are very useful because they are carried out by a multidisciplinary group of professionals dedicated to finding the keys to the best medical care for children and adults with PTLS. Our team has evaluated over a dozen individuals with PTLS, and while we do not have all of the answers, we have more insight because of our experience. See our website www.bcm.edu/genetics/dup17p11.2/index.html or contact Dianne Dang or Patti Robbins-Furman for more details about these research studies.
Healthcare Guidelines for PTLS

Potocki-Lupski syndrome (PTLS) is a chromosomal duplication syndrome (duplication 17p11.2) with an incidence of at least 1 in 20,000. Most individuals with PTLS have only mildly dysmorphic features, thus a chromosomal abnormality is often not suspected clinically. Of the patients we have evaluated in the General Clinical Research Center at Texas Children’s Hospital most children diagnosed with PTLS presented with developmental delay, speech and language delay, and autistic-like behavior. Other common features of PTLS (seen in 70%-100% of patients) include failure to thrive, oral-pharyngeal dysphasia, hypotonia, abnormalities on electroencephalogram, hypermetropia (farsightedness) on ophthalmic examination, and sleep disordered breathing. Structural cardiac anomalies have been observed in nearly 50% of patients and include septal defects, bicuspid aortic valve, dilated aortic root, and hypoplastic left heart.

The following general guidelines are intended to assist physicians and health care providers in determining the best care for individuals with PTLS and can never replace good clinical judgment and practice. Most of the studies below should be followed and re-assessed as your child grows and develops. Any abnormalities should be addressed and managed as medically indicated.

- Feeding evaluation; assessment for failure to thrive if applicable
- Developmental assessment
- Autism spectrum disorder assessment (ADI and ADOS)
- Speech and language assessment
- Ophthalmological examination
- Otolaryngological examination (ENT)
- Audiological examination
- Echocardiogram with evaluation of the aortic root
- Electrocardiogram
- Renal ultrasound
- Sleep study (to assess for sleep apnea)

On-going therapies should include:

- Speech and language therapy
  With consideration for augmentative communication.
- Physical therapy
  With consideration for adaptive physical education
- Occupational therapy

For further information please see the full article published in the American Journal of Human Genetics (Am J Hum Genet vol 80: 633-649, Apr 2007), or contact: Lorraine Potocki, M.D., F.A.C.M.G. at lpotocki@bcm.tmc.edu.

After The Diagnosis

Patti Robbins-Furman, M.P.H.
Certified Genetic Counselor

For some families, the diagnosis of duplication 17p11.2 in their child comes after searching for answers for many years. Finally having a diagnosis or name for their child’s disorder may be somewhat of a relief after years of consulting with multiple specialists and undergoing multiple tests. For other families, especially those who have very young children, the diagnosis of this chromosomal duplication may be made as part of their child’s initial evaluation.

Being confronted with the reality of a specific diagnosis in a child is a shock to many parents and may initially be accompanied by feelings of grief and despair. Whether you are a parent or a grandparent whose child has just been given this diagnosis, or if you have known about the diagnosis for some time... the diagnosis of PTLS may leave you wondering, “what do we do next?”

It is important to know that having a diagnosis of PTLS does not change who your child is or what he or she can and will accomplish. But having a diagnosis and cause for some of your child’s symptoms may facilitate obtaining needed services. It is also completely natural for parents to search for things they may have done or not done that may have led to their child’s diagnosis. Knowing that chromosomal abnormalities are beyond our control may help lessen normal feelings of guilt and empower parents to move forward in advocating for their children.

One of the goals of the ongoing clinical study regarding PTLS is to find out if any seemingly random birth defects or health problems may indeed be related to the chromosomal duplication. This is one way we can help families with a new diagnosis of PTLS know what specific health concerns are present. A structural defect of the heart was seen in more than half of the children, published recently (Potocki et al, 2007). Therefore, it is suggested that any child with a new diagnosis of PTLS have an echocardiogram. Most children in the study had some features of autism spectrum disorder. Since there is
a wide spectrum of these features, a detailed evaluation specifically for autistic features is warranted. This can be very valuable information for a family when planning educational and behavioral interventions for their child.

Early intervention therapies such as speech, occupational, and physical therapy are important. Some children with PTLS will benefit from augmentative communication devices. Many children with PTLS have feeding problems and food/texture aversions. For some children the feeding problems will get better with age. Seeking advice from other parents who have faced some of these issues with their children may often be the best way to tackle problems such as food aversions. A sleep study and EEG is also part of the recommended work-up for children with PTLS. Although seizures are not a hallmark of PTLS, many children have abnormalities on EEG and may be more prone to have a seizure under certain conditions. For example, some medications may lower the seizure threshold in children. Since children with PTLS may be more prone to developing seizures, these medications should be avoided.

Since PTLS is a relatively newly recognized disorder, many health care providers and teachers do not know much or anything about PTLS. As parents, you will likely need to educate your child’s specialists, teachers and caregivers. Hopefully, being armed with a diagnosis, a copy of the Potocki et al paper, and the PTLS parent group, the road to better health care and successful education strategies will be smoothly paved and well lighted!

RESOURCES
Genetic Alliance: http://www.geneticalliance.org
Duplication 17p Yahoo support group: http://health.groups.yahoo.com/group/Dup-17p11-2/
NORD (National Organization for Rare Disorders): http://www.rarediseases.org

©Positive Exposure
Comes to Houston

Baylor College of Medicine and Texas Children’s Hospital were very fortunate to welcome photographer, Rick Guidotti to Houston. Rick was invited to participate in the Compassion in the Art of Medicine lecture series at BCM. We widened the scope of his visit to include a fabulous photo exhibit of his work as well as a mini PTLS family get-together and photo shoot.

Four PTLS families attended the photo shoot and reception. The younger children, Adan and Allison, had a great time running around and doing what 4 year olds do, while Christian and Stacey, both in their 20s enjoyed sharing their interests and stories.

“I had a lot of fun meeting more families that have kids with the same syndrome as my son. My son had a blast!”
– Mom of Adan, age 4

“The visit was an excellent opportunity for me to be able to put a face to a person I have been talking with. I believe Christian helped to answer some questions as well as give comfort to those families by getting a glimpse of the possible future they could have.”
– Mom of Christian, age 20.

“It was nice to know that I had people who were like me and had the same duplication that I have. I am proud to be a role model, with Stacy, for them. It was fun having my picture taken. I felt like a model. It was good tears that Dr. Potocki cried when I made a comment to her. I think I was a big help talking to the other families and speaking on the panel [at the Compassion and the Art of Medicine Seminar]. I know I made a difference being able to talk on the panel because [the medical students and doctors] came up to me and thanked me.”
– Christian
Saddle up and ride on down to Houston Texas in June 2009 for the PTLS Family Conference.

Families, friends, healthcare professionals and educators are invited to attend. We are looking forward to a program with guest speakers including Drs Potocki, Lupski and Treadwell-Deering; small group discussion sessions with parents and our speech pathologist Anna Eifert and psychologist Paige Powell; and kicking back with dinner and fun activities with attendees and speakers.

The planning process has just begun! To get involved or if you have questions or ideas please contact Patti Robbins-Furman at pattif@bcm.edu or call 832-822-4281.