Hello everyone. Hope you are all having a wonderful summer – enjoying family vacations, and with any luck, a slower pace during these warmer months. To that end, if you do have time, check out the Book Corner below. All our recommendations are focused on the many mysteries of genetics…. interesting and absorbing reading. We are also pleased to introduce you to CDO’s newest contributor, Molly Zenk; her first byline, Back to School Tips, appears in this issue. Meet our Featured Family, the Nichols and their daughter, Gracyn, in this issue too. And finally, the most exciting news – our new website launch is planned for September. This has been a long, very involved process and we are thrilled to finally be able to present all the upgraded functionality this new site will offer. So please visit CDO online this September and tell us what you think! All the best, Linda Sorg

**The Boy Who Loved Too Much: A True Story of Pathological Friendliness** by Jennifer Latson
The poignant story of a boy’s coming-of-age complicated by Williams syndrome, a genetic disorder that makes people biologically incapable of distrust.

**The Family Gene: A Mission to Turn My Deadly Inheritance into a Hopeful Future** by Joselin Linder
A riveting medical mystery about a young woman’s quest to uncover the truth about her likely fatal genetic disorder that opens a window onto the exploding field of genomic medicine.

**Mercies in Disguise: A Story of Hope, a Family’s Genetic Destiny, and the Science That Rescued Them** by Gina Kolata
New York Times science reporter Gina Kolata follows a family through genetic illness and one courageous daughter who decides her fate shall no longer be decided by a genetic flaw.
BACK TO SCHOOL TIPS FOR SPECIAL NEEDS FAMILIES

For many people there’s a rhythm to back to school shopping. It’s a time for new books, clothes, friends, and adventures. What if you’re the parent of a special needs child? Instead of excitement, you might be anticipating anxiety, chaos, and challenges. What is a fun time for families, becomes a long line of hurdles for those with special needs.

There’s a saying: "prepare the situation for the child and prepare the child for the situation." This works well for the back to school mentality. It can be sensory overload. Everyone looking for the same list of school supplies. Not knowing how much patience your child may have to clothes shop. How are you going to survive? It can be a stressful time for everyone in the family, but it doesn’t have to be. Here are some tips on how to make back to school shopping as stress-free as possible:

1. Honor your child’s feelings. Any adults out there are veterans of back to school shopping. We know what it’s like. It can be scary, too bright, too loud, too a million different things that can cause sensory overload. If your child is done, go. Come back another day.

2. If your school has a list of school supplies available online or in store, print it out and plot your game plan. The more prepared you are, the better. It also means you can get in and out of the store faster. Many stores have their school supplies located in one section. This makes it much easier to find what you need.

3. When it’s time to shop for clothes, show your child pictures online beforehand to see if you can get a "yes" or "no" reaction. You should already know their size, favorite characters, favorite colors, and favorite textures. Shopping online is an option. If not, go armed with as much information as possible. Be prepared to leave if you notice your child getting bored or ready to melt down. Clothes shopping -- like school supply shopping - can happen in short trips instead of all at once. Don't exhaust or overtax your child. Know their limit...and yours.

4. Take your child to their classroom open house before school starts. This is a great way to meet the teacher and staff, explore the classroom and school layout, and ask questions. It is a great time for everyone to get comfortable.

Preparation is key to having a successful back to school experience. By knowing what to expect, your child will feel more comfortable and confident. They’ll have a positive, happy, healthy, less stressful school year. Isn’t that what everyone wants for their child?

— Molly Zenk is a writer and mom to 3 girls with 3q29 duplication
FAMILY SPOTLIGHT: GRACYN NICHOLS, 18P-20P+ TRANSLOCATION

My daughter Gracyn was born August 11, 2014. We knew something wasn’t going to be right from the time I was 16 weeks pregnant, the perinatologist told us that she had a bright spot on her heart, which was an indicator for Down Syndrome. We went forward with Harmony testing to see if any syndromes showed up, it came back negative. At my 20 week appointment Gracyn’s ventricles in her brain were severely enlarged, the doctor told me she had aqueductal stenosis and possibly hydrocephalus. I was monitored closely throughout my pregnancy and by the end, her hydrocephalus was downgraded to mild ventriculomegaly. I was induced, just to be prepared for whatever could be, she was 6lbs11oz and her birth was uneventful. They performed an ultrasound of her brain before we left the hospital and said that her ventricles were moderately enlarged.

We took our newborn princess home and she was adored by her two older brothers Gavin who was 14 at the time and Garrett who was 10 at the time. She was jaundice, so we took trips back and forth to the hospital and doctor to check her levels. I knew something was different, but I just tried to get used to being a mom of a baby again. At two months old, her pediatrician ordered a follow up ultrasound of her brain. The day after her ultrasound they called and wanted us to do an MRI, little did I know at the time they thought she did not have a corpus callosum. They ended up saying she had moderate ventriculomegaly and a very thin corpus callosum. We were referred to a neurologist and a neurosurgeon at this time. The neurosurgeon decided to do a sedated MRI around 7 months old, her ventricles were large but stable.

When Gracyn was eight months old, we started with a new neurologist, he found several genetic markers. He ordered a microarray and several other tests, at the time I had no idea what any of it meant. When I received the call, my heart went to my stomach as he let me know that my daughter has a chromosome translocation 18p-20p+, he referred us to Emory Genetics to find out everything we could about our sweet baby. Emory could not tell us much because Gracyn is “one of a kind”. I have since found five other people on my own with the same translocation, but their breaks in the chromosomes are different and so are several of their symptoms. I remember having thoughts such as, “What did I do to cause this to happen to her?”, and “My daughter does not deserve all of this madness!”. Sometime in the midst of the fog we had entered as a family, she started to receive physical therapy, this is when you wake up and realize how far behind in milestones your child truly is. She could not sit on her own, her head had tilted so much that her left cheek was fuller and her features were drifting with the tilt. She had to go to an ENT around 11 months old, who recommended tubes, but also discovered that she has a bifid uvula and a submucous cleft palate. I have changed doctors and therapists when something hasn’t felt right, making sure she has the best care possible, has become my goal for her.

Life has continued as normal as possible since we have found out everything. My boys have still been able to play sports and do activities, we take vacations and do day trips. The boys are 17 and 13 and Gracyn will be three in August, my oldest son will be a senior this year and I homeschool my middle child. I am also trying to get Gracyn into the special needs Pre-k program in our county. We see a team of seven doctors and five different therapist. Gracyn’s diagnosis are: 18p-20p+ translocation that causes (idiopathic) non-pressure hydrocephalus, thin corpus callosum, rotated hippocampus, submucous cleft palate, hypotonia, dysphagia, and global developmental delays. But all of those are just words, our pediatrician of 17 years told me,” just don’t hold her back”, so I don’t. I push her as hard as she will let me to meet her goals and still have fun. Our lives are not over since we had our special princess, they are just different. She makes me a better person, a more patient person, a person who will stop now to admire a rock or a flower. I love getting to see the world through her innocent eyes. My sweet Gracyn is climbing mountains daily, and I am so thankful that I was chosen to hold her hand all the way to the top.
Having a child, loved one, or friend face a diagnosis of any medical condition can be a daunting, often terrifying, experience. What happens when that diagnosis is a rare chromosome disorder? Who do you turn to for advice, information, and understanding? For over 25 years, Chromosome Disorder Outreach (CDO) has been that voice and support for families. Now we need your help to achieve our fundraising goal for a very special project: CDO’s Database Registry.

Once a family receives a diagnosis and finds their way to us through a web search, doctor’s office, or word of mouth, they register their information in the CDO database. This allows families to connect with others around the world with the same rare disorder. It also allows CDO to keep a detailed record of the chromosome disorders and helps researchers and geneticists understand more about the rare disorders. The CDO motto has always been: You Are Not Alone. The database is the realization of that dream.

Unfortunately, maintaining the database system and security is an expense that our small nonprofit cannot do alone. That’s where you come in. For the entire month of September, we are raising funds for a new database registry management system. Won’t you help us continue to help you?

Visit generosity.com and search “chromosome disorder outreach” or click on https://www.generosity.com/community-fundraising/chromosome-disorder-outreach-september-giving-days
New Research Abstracts

Complete listing of all recent new research abstracts are accessible on our website. Full texts of some articles mentioned may also be available.

Simply email info@chromodisorder.org for more information.

Functional monosomy of 6q27-qter and functional disomy of Xpter-p22.11 due to X;6 translocation with an atypical X-inactivation pattern

In females, because there are 2 X chromosomes, one of them undergoes a phenomenon of X-inactivation where it becomes silenced and is not expressed. The chromosome that becomes silenced in each cell is usually random. However, when a translocation involving the X chromosome occurs, the structurally abnormal X chromosome is usually preferentially inactivated. If, due to translocation, the autosomal segment is replaced onto the X chromosome, inactivation may also spread to this autosomal segment. As a result, the patient may have a functional monosomy for the inactivated part of the autosome (usually with functional disomy for the segment of X-chromosome), even though he/she may have a formally balanced karyotype.

The authors describe a girl with significant developmental delay, microcephaly, hypoplastic cerebellar vermis, neuronal heterotopias (abnormal neuron migration), ventricular septal defect and facial dysmorphology (bilateral epicanthic folds, wide nasal bridge, broad nasal tip, broad philtrum, thick and everted lower lip). The girl had a cytogenetically balanced translocation t(X;6)(p22.11;q27), but the derivative X chromosome was inactive in all cells. Spread of inactivation to the part of 6q explains the clinical abnormalities in this patient. Functional disomy Xpter-p22.11 is most likely not responsible for the clinical manifestations in this patient. The girl also had a microdeletion in 6q21, involving only two genes, but this microdeletion is most likely a benign variant.

Comprehensive genomic and phenotypic characterization of germline FH deletion in hereditary leiomyomatosis and renal cell carcinoma

Hereditary leiomyomatosis and renal cell carcinoma (HLRCC) is a cancer syndrome that is caused by mutations in the FH gene in 90% of cases. In the other 10% of cases, the genetic cause is unknown. Here, the authors examined 28 patients from 13 families where no point mutation in FH has been found. These persons were screened for abnormalities that involve the FH gene. They discover that all 13 families carry deletions of chromosome 1q42, the region where FH is located. Eleven of the families have a full deletion of the FH gene and two families have a partial deletion. All 13 female patients (100%) from 7 different families had uterine leiomyomas. There were no female patients identified in the families with partial deletions so they were unable to determine if the partial deletion could cause uterine leiomyomas. Twenty patients were examined for cutaneous leiomyomas, and 18 of them (90%) were found to have this type of cancer. Cutaneous leiomyomas were found in families with full deletions or with the partial deletions. Finally, there were 9 patients (from 7 families) with kidney cancer, and it was associated with both the full deletions and the partial deletions. Most individuals (8 of 9) had type-2 papillary renal cell carcinoma, which is common with HLRCC. The percentage of patients presenting with each feature is very similar to what has been described for patients with point mutations in the FH gene. Deletions of 1q42 involving all or part of the FH gene is a genetic basis for HLRCC in the families where no point mutation in the FH gene is found.

Prevalence of hearing loss and clinical otologic manifestations in patients with 22q11.2 deletion syndrome: A literature review

Microdeletions of 22q11.2 frequently lead to hearing loss and recurrent otitis media (ear infections). The 22q11.2 deletion syndrome can lead to difficulties in speech and language, underscoring the importance of identifying hearing defects early in these individuals. To determine the frequency of hearing loss and otitis media in 22q11.2, the authors performed a literature search to identify all studies that report on ear problems in 22q11.2 individuals. They found 25 articles that addressed hearing loss and chronic or frequent ear infections in 3381 individuals. They found that the overall rate of hearing loss from 21 studies ranged from 6.0%-60.3%. Conductive hearing loss was the most common form and was prevalent in 5.6%-53% of individuals. Sensorineural (0%-19.4%) and mixed hearing loss (0%-28.2%) were also found, however, they were not as common as conductive hearing loss. Recurrent ear infections were found in 2.2%-89.8% of individuals in 21 studies. They found that the incidence of hearing loss and recurrent ear infections was higher in 22q11.2 deletion syndrome than in the general population and this may be due to structural defects in the ear. Interestingly, people with cleft palate often have chronic ear infections, and cleft palate is a common feature of 22q11.2 syndrome, indicating that these two features may be linked by a common structural defect. Taken together, this review highlights the frequency of hearing loss and chronic ear infections often found in 22q11.2 deletion syndrome and that individuals with this syndrome should undergo regular check-ups with a hearing specialist.
**QUESTION:** 14 and 22: My Karyotype is 45,XY,rob(14,22) (q10,q10). My wife’s is normal. We had two miscarriages. What is the reproductive risk to have a normal child? I have heard that translocation relating to chromosome 22 will impact to blood cancer is that correct? I’ve heard that translocation relating to chromosome 22 will impact to blood cancer is that correct?

**ANSWER:** Robertsonian translocations t(14;22) are exceptionally rare and there is no empirical data about reproductive risks for the carriers. Theoretically, there is a ~50% chance of having a balanced sperm with translocation or a normal sperm, and the same risk of unbalanced sperm with disomy 22 or disomy 14. All embryos with trisomy 14 and 99% of embryos with trisomy 22 will not survive, producing a miscarriage. Basically there are two options: a) try to conceive naturally with a 50% chance of a miscarriage or b) selection of normal sperm-cells for in vitro fertilization.

Regarding the risk of malignancies: patients with CONGENITAL translocations involving chromosome 22 have the same risk of malignancies as the persons with a normal karyotype. ACQUIRED translocations typical for some blood malignancies are unrelated to CONGENITAL translocations.

**QUESTION:** arr[hg19] 1q21.1(145,390,156-145,888,926)x3: I would kindly ask for your experience and knowledge regarding the above CMA test results obtained during the 13th Week of our first pregnancy: What should we expect? What do statistics say? What are the current recommendations in this case?

**ANSWER:** Most duplications of this kind are innocent familial variants. I recommend testing of both parents. If one of them is found to be a carrier we will have all reasons to consider this duplication as innocent. If however the duplication is sporadic it may increase the probability of some abnormalities in the fetus (or more likely in a child).

Information contained on this website or in any electronic or written communication should be used for supplemental purposes only. We urge patients and their families to always check with their personal healthcare provider first with any questions or concerns. Your doctor is most knowledgeable about your personal situation. Please see chromodisorder.org to review our privacy policy.