WINGS

WAGR Information, News, Gorilla Stories

IWSA
PO Box 392
Allen Park, MI 48101

Spring/Summer 2012

www.wagr.org

From the Chair

Dear Families and Friends,

July is just a few months away so that means WAGR Weekend is right around the corner. A number of WAGR families have already replied with an RSVP via the www.wagr.org website. The SpringHill Suites has given us a great group room rate of $69.99/night for Double/Double. Rooms are limited so you will want to make your reservation soon. You don't want to miss out on this fabulous one of a kind weekend event. Our featured guest will be Dr. Joan Han and the NIH team who will be making a presentation to parents on Saturday. Please feel free to contact Shari Krantz at classicshari@yahoo.com with any questions.

WAGR Weekend financial assistance is still available for any family that would like to join us in Gaithersburg this summer but who may not have the financial means to do so. Please contact Tammie Hefty at tammiehefty@yahoo.com before April 30th for more information.

This year's fundraising efforts have gotten off to a great start thanks to the staff and students in the Riverview School District in Michigan. The December Casual Clothes for a Cause day raised over $1,000 for the IWSA. We are greatly appreciative for the support we have received from the RSD over the past few years.

We were sad to hear that we were not granted the Community Award Grant from the March of Dimes for 2012. This means we have a $1,200 shortfall in our Operating Budget. The money we received from the March of Dimes Grant went to offset a portion of the printing/mailing expense for *WINGS*.

We will be holding our Second Annual Summer Sizzling 50/50 Raffle this summer. The drawing will take place on Saturday, July 21st during WAGR Weekend. Tickets will be sold for $5 each. We have included five tickets with this newsletter. You can help us by selling the five tickets or by purchasing the tickets for yourself. Just return the ticket stubs and a check for $25 made out to the IWSA in the self-addressed envelope. If every family would sell/purchase just five tickets we could easily raise enough money to cover the March of Dimes Grant shortage. Please contact me by email for additional tickets if you want to purchase or sell more. There will be a prize awarded to the family or individual who sells the most tickets. Ticket stubs and money need to be postmarked by July 11th, 2012.

Annie Prusakiewicz, TheMooZoo@aol.com

Inside this issue:

Think Spring and help the International WAGR Syndrome Association too!

By participating in our FlowerPower fundraiser you can help us reach our goal of $1,000. Fifty percent of all sales go to the IWSA. Place your order by going to the FlowerPower link on the www.wagr.org website. The flowers will be shipped directly to your home. **Contact Shari Krantz**–classicshari@yahoo.com with any questions. The fundraiser end date is April 27, 2012.

The mission of the IWSA is to:

- Promote International knowledge and awareness of WAGR/11p Deletion Syndrome and its complications and treatments
- Stimulate Research
- Reach out to those affected by WAGR/11p Deletion Syndrome in an effort to improve their lives

The IWSA is a nonprofit 501(c)(3) organization.

All donations are tax deductible.

Our Story

By Keri Skitch

Alex, Megan, Sophia, Keri & Anna

My name is Keri and I am writing from northern Spain. My husband (Alex) and I are a Spanish/Canadian couple with three girls. Sophia, who is six, and the twins; Anna and Megan who are two. Our WAGR story began over two years ago.

"Life has radically changed of course, and we mostly just look towards the future"

Keri Skitch

Megan was born in December 2009 and it's hard to believe it's already been over two years. The first days and weeks (make those months!) were challenging to say the least. The fact that she is a twin made it even more so. Her sister, Anna, came home with me from the hospital after one week, in good health. However, Megan stayed for a total of five weeks. It wasn't easy to balance the care of a baby at home, her older sister, and get to the hospital every day to see Megan. Luckily my recovery was surprisingly quick and I'd heard that a second caesarean is easier than the first; which was certainly true in my case. Fortunately Sophia was a good sport and loving big sister from day one, and I was able to count on my mother's help. Alex took as many days off work as he could.

Anna and Megan, Spain

We managed to get through the first few months without sleep somehow. It was non-stop feeding, diapering, etc., and all the while sorting out all the new information bombarding us. I think every test in existence was performed on Megan. At every appointment we knew when it was our turn since her file was triple the size of the other babies. We watched the Vancouver Olympics live from Canada while feeding the babies in the middle of the night, as we were living in Holland at that time. Watching 'the women's skating final' or 'pair's semi-final' at 3 a.m. got me through many nights!!

We found out during my pregnancy that something wasn't right. It was week 27 or thereabouts that I went for a routine scan. Because I was having twins, it was recommended that we not do an amnio due to the higher risks involved and we agreed. However a routine ultrasound showed that one of the twins' limbs were shorter than usual. It also showed that she had agenesis of the corpus callosum, which means that the connection between the two hemispheres of the brain isn't there. We were then told through more testing that it was likely a Trisomy 18 and that we would probably lose the baby. Of course this was a total shock. Until that point we had imagined the craziness of having twins, them playing together, entertaining each other. We began to accept that we would lose one, but took some solace in the fact that we would still have the other. It was very bittersweet. Unfortunately, it took away any excitement about being pregnant. During this time the few friends we had around us shared many stories; many stories about those who had miscarried and lost their baby late in pregnancy. Something that isn't talked

about very much, but affects so many women. This was a real eye-opener for me. We tried not to worry but there was an awful lot to think about. Right up to the day of the birth, I had prepared myself to take photos of the babies together, even if one was stillborn.

The fighter that she is, Megan wasn't having any of that. She was born with a nine on the Apgar scale and was whisked away to the neonatal room along with her sister. At only 1.665 kilos, Megan was just a tiny thing; full of tubes and so on right from day one. Her sister at 2.1 kilos was also tiny but fattened up quickly. Megan took much longer, with her tiny body and nasal tube feedings. Little by little she took the bottle and was able to switch to bottle-only feedings by the time we took her home. That was a special day! We didn't think we'd have two babies at home. But our twins were at home; sleeping side by side after all!

The medical system in Holland was fantastic. Their rapport with patients was excellent; they never finished an appointment without asking 'do you have any more questions?' We were never rushed out the door. By about four weeks old, Megan's genetic analysis was complete. She had two diagnoses, both 11p: WAGR and Potocki-Shaffer syndrome. The protocol was set immediately for regular kidney ultrasounds, every three months, and ophthalmologic exams every 5-6 months, which continues today.

I feel lucky that we knew something was going on, that we had a diagnosis so early. I think it suits both my and my husband's personalities, to know what's happening, even if it's scary. I think of the families in the past who didn't know what was wrong, and had to wait months, years or even decades before getting an accurate diagnosis. I am grateful for the excellent team of doctors, who helped us through that, especially our pediatrician who was as kind and caring to us as a family during those first months. There were and still are many very, very difficult days, where I just need to get through the day. Sometimes we feel depressed and upset, asking 'why us?', but it's usually because we are more tired than normal, and it passes. I am still working on my coping mechanisms.

Fast forward to 2012. Megan has developed very little; she is still much like a newborn. She is very small, but that works in my favor as I can hold her and carry her around at only eight kilos. She doesn't sit or roll over, but her head control has improved as has her hand control. We are working with occupational- and physiotherapists every week to get her to look at and manipulate objects. Her vision is poor; though we have glasses for her myopia, we think she only sees light and shadows. We are working on finding out what she can and cannot see. She attends daycare for a few hours a day with her twin sister. This gives me a break. The staff at the day care are loving and interested and have made advances with her in terms of spoon feeding which is something I haven't managed myself. Because of her hypotonia, she has difficulty coughing up phlegm, which has led to numerous bronchial infections over the last year. Despite all her challenges, she is a happy little girl. When she isn't fighting a cold or infection, she is content and happy just to be held and talked to. She is a superhero, as far as being a patient is concerned; she lets us give her any and all treatments she might need without complaint. The serious expression she usually wears is broken frequently by hilarious giggling fits. Yes, Megan giggles! It makes us all crack up. It's as if she has some secret joke, that suddenly makes her burst into uncontrollable fits of laughter. You'll see what I mean when you meet her.

She has opened our eyes to another world. Life has radically changed of course, and we mostly just look towards the future. We try to not look at the 'what ifs', what would be the point? Megan is Megan. She is loved greatly by her sisters, and by all of the family. As Barbara Gill talks about in her book, 'Changed by a Child', I would define Megan as a 'cuddly'. Let us not look at what they are not or should have been, but rather accept that there are three kinds of children: boys, girls and cuddlies. Well, in our family we have a cuddly. And her name is Megan.

Genetics 101

By Katrina L. Epperson, BA and Joan C. Han, MD

Understanding the role of genetics in diagnosis, treatment and management of diseases like WAGR/11p Deletion Syndrome can be confusing and overwhelming for many of us. The information presented here is intended to provide some of the basics of genetics and how they relate to our loved ones.

1. What is DNA?

-DNA carries the genetic information for all living organisms. DNA is composed of four different nucleotide bases. The nucleotide bases are Adenine (A), Guanine (G), Cytosine (C), and Thymine (T) and function like a miniature alphabet. Unique combinations of bases provide the instructions or 'words' the body uses as the blueprints for biological development and function.

English alphabet: A B C.... X Y Z

DNA alphabet: A C G T

2. What is a gene?

-A gene is the way we inherit the biological instructions or 'words' needed for development and function. It is made up of DNA, the 'miniature alphabet', which encodes proteins needed for human life.

English words: bread and butter

DNA words: GCT ACC

3. What is a chromosome?

-Chromosomes are the way we package and store DNA and the genes they encode in our cells. Chromosomes are like books with many different chapters. The chapters are bands in the chromosome that can encompass many genes or "words." Each person has 23 pairs of chromosomes or "books." Half of the DNA is inherited from the mother and the other half from the father for a total of 46 chromosomes (23 pairs).

4. How are specific genes labeled?

-The labeling system is equivalent to an index or table of contents. All chromosomes or "books" are identified by a number (1-22) except for the last pair. The last pair of chromosomes is the sex chromosomes, which determine whether a person has male or female characteristics. Males have one X and one Y chromosome and females have two X chromosomes. Every chromosome is also organized into two arms, one that is short and one that is long. The arms are connected by a centromere. The short arms are identified with the letter 'p' and the long arms with the letter 'q.'

When a gene is labeled, the specific "book" must be identified followed by identification of the arm of the "book," and finally the specific "chapter" of the "book." For example, in WAGR/11p Deletion Syndrome, there is an 11p13 deletion (see question 9 for a description of deletions). This means the deletion occurs in chromosome, or "book," 11 on the short arm (p) in band or "chapter" 13. People with 11p deletions can also have deletions that involve genes in chapters 12 and 14 (designated as 11p12 and 11p14).

5. How are genes inherited? What gives people their individual characteristics?

-An individual receives half of his or her genes or "words" from the mother and the other half from the father. Each person will express a unique set of traits based on the distinct combination of genes. Slight variations in spelling are what allow for there to be differences in traits and characteristics among people.

gray vs. grey

6. What is the human genome? What is the Human Genome Project?

-The human genome is a person's complete set of DNA packaged into chromosomes inherited from the mother and father. The Human Genome Project was an international effort to determine all the genes needed for human life. The project was started in 1990. In 2003, the genome was mapped to 99.99% accuracy. Since then, further updates have been made to fine-tune the accuracy. Having knowledge of the entire human genome gives researchers the equivalent of an instruction manual for the human body. This instruction manual is helping us guide our understanding of medicine,

biology, social sciences, and bioengineering (along with many other fields of study). Genetics is a very new field of study that began a little over 100 years ago with the discovery of genes in the 1900s. It is rapidly changing our understanding of the human body and constantly improving medical care.

7. How many genes are in the human genome?

-There are about 3 billion base pairs that make up the DNA of the human genome. There are approximately 25,000 genes, accounting for only 2% of human DNA. The rest of the DNA includes sequences that do not make proteins or are repetitive, but these regions may be important for controlling the function of the genes. The function of over 50% of genes is still unknown, but ongoing research aims to determine their purposes.

8. What is a genetic mutation? What does *de novo* mean?

-A genetic mutation alters the "letters" of DNA. If it is not repaired, this can potentially cause various problems in the individual depending on which gene or "word" is changed. These mutations can be inherited from a parent or can occur as a new mutation that is not inherited from the parents (*de novo = Latin for "from new"*) due to a variety of different factors including the environment or a spontaneous event with no known cause.

9. What does it mean to have a deletion or haploinsufficiency?

-A deletion is a type of mutation where there is a loss of genetic material or "words." This loss can be very small, involving only one nucleotide base or "letter." It can also involve larger deletions, such as losing a whole "paragraph" or "chapter" of a chromosome. Each person has 2 copies of every gene, one from the mother and one from the father. Haploinsufficiency refers to the loss of function of 1 copy of a gene. This can be caused by deletion of the gene or due changes in the "letters" of DNA resulting in a "misspelling" that causes protein not to be made by that copy of the gene.

10. What is WAGR/11p Deletion Syndrome?

-WAGR Syndrome is a rare genetic disorder predisposing individuals to four main categories of disease:

Wilms tumor- the most common form of kidney cancer in children

Aniridia- partial or complete absence of the colored part of the eye

Genitourinary problems- examples include undescended testicles or abnormal opening for urination in males (hypospadias) or uterus and ovary problems in girls

Cognitive ImpaiRment- some patients have varying degrees of intellectual disabilities

-WAGR is the result of gene deletions in the area of chromosome 11p13. This deletion is most often the result of a sporadic (random) *de novo* (not inherited from the parents) mutation due to an unknown cause. The deletion is heterozygous and dominant. This means that only one copy of the genes in the 11p13 region is deleted. The other copy of the genes is fine, but loss of one copy of the genes is enough to cause health problems.

11. What are the gene deletions seen in WAGR/11p Deletion Syndrome?

-The number of genes deleted on chromosome 11p13 varies from patient to patient. In our study at the NIH, we have found deletions ranging from 1 million to 26.5 million base pairs. The average size was approximately 11 million base pairs. Deletion of *PAX6* and *WT1* are common among patients who share the classic features of WAGR/11p Deletion Syndrome. However, each patient is unique and may have deletion of different additional genes. Some patients with 11p deletion do not have *PAX6* and *WT1* deletion, and their condition is usually referred to as "11p deletion syndrome." WAGR/11p Deletion Syndrome is considered to be a subtype of 11p deletion syndrome.

12. What are some of the clinical differences seen in patients with different deletions?

-Depending on each patient's unique set of gene deletions, this predisposes him or her to different health problems. Deletion of *PAX6* is associated with andiridia. Deletion of *WT1* is associated with Wilms tumor and genitourinary problems. Deletion of *EXT2* is associated with bone tumors, called osteochondromas. Deletion of *ALX4* is associated with abnormal holes in skull. Deletion of *BDNF* predisposes to obesity and higher pain tolerance.

13. Is it helpful for patients with WAGR/11p Deletion Syndrome to know their specific deletions?

-Yes, knowing their specific deletions helps guide clinical care. For example, if a physician knows that *EXT2* is deleted, monitoring for the bone tumors with exams and X-rays can be initiated. If a physician knows that *BDNF* is deleted, extra counseling about weight management can be provided during infancy before obesity occurs and more attention can be paid toward monitoring growth to help prevent excessive weight gain. Also, knowing that *BDNF* is deleted may alert physicians to be more cautious when the child complains of pain because having a higher pain threshold could mean that very serious illnesses, like pancreatitis, could manifest with milder symptoms. Researchers are conducting studies to learn more about the functions of all the genes that can be deleted in WAGR syndrome. We hope that by knowing more about the function of the deleted genes, patient care can be improved.

14. Are there any downsides to knowing which deletion a patient with WAGR/11p Deletion Syndrome has?

-Yes, there can be some downsides to knowing which deletion a patient has. Because still we do not know the function of many genes, knowing the deletion can sometimes lead to worry about unknown possibilities. Also, even if the functions of genes are known, identifying the deletion may not help prevent disease because treatments are still not known. There are also cases where none of the symptoms associated with the deleted gene are present yet and it is possible they may never show up, but knowing about the risk can cause worry and extra testing. Additionally, while health insurance cannot be denied based on a genetic condition, under current laws, disability and life insurance can still be denied. We advise that families discuss the pros and cons of genetic testing with their doctor or a genetic counselor prior to genetic testing.

15. Can an individual with WAGR/11p Deletion Syndrome pass the disease on to their children?

- Yes, a person with WAGR/11p Deletion Syndrome can potentially pass the traits of the disease onto children. Most people with WAGR/11p Deletion Syndrome did not inherit the 11p deletion from their parents because the mutation arose *de novo* (see question 8). However, once the deletion is present in a person, there is 50% chance of passing on the deletion to each of his or her children.

16. Which genetic tests can determine a patient's deletion?

-Genetic testing is a DNA-based lab test used for diagnosing genetic disorders. Most genetic tests require a blood draw, typically less than a tablespoon of blood.

Three main types of genetic tests can be performed to characterize deletions associated with WAGR/11p Deletion Syndrome, including:

1) *Karyotype*- provides an overview of the size, shape, and number of chromosomes, and can identify fairly large deletions, but can miss smaller sized deletions
2) *Fluorescence in situ hybridization (FISH)*- uses fluorescent probes to specifically detect the absence (or presence) of a specific gene
3) *Comparative Genomic Hybridization (CGH)*- allows detection of regions of gene deletion or duplication with much better precision than karyotype and provides somewhat similar information as FISH, except it allows for testing of many genes at the same time

17. Is genetic testing covered by health insurance?

-Most genetic testing is covered by health insurance. First, check with your health insurance provider to learn which tests are covered. The NIH also offers free genetic testing for participants in certain research studies.

18. How do genetics help further treatment and research for WAGR/11p Deletion Syndrome?

-Determining the genetic basis for disease is crucial to the understanding of why each patient has certain symptoms and can guide physicians in monitoring, preventing, and treating diseases. The goal of learning more about genetics is to improve the quality of care and life for patients with WAGR and other 11p deletion syndromes.

To learn more about genetics and WAGR/11p Deletion Syndrome, the following resources that were used to prepare this article are available online:

National Human Genome Research Institute: Learning About WAGR Syndrome

http://www.genome.gov/26023527#al-1

- *National Organization for Rare Disorders: WAGR Syndrome/11P Deletion Syndrome*

http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/1014/viewAbstract

- *National Institute of Health: Genetics Home Reference*

http://ghr.nlm.nih.gov/condition/wilms-tumor-aniridia-genitourinary-anomalies-and-mental-retardation-syndrome#definition

- *Human Genome Project Information*

http://www.ornl.gov/sci/techresources/Human_Genome/faq/faqs1.shtml

About the authors: Ms. Epperson is a first-year medical student at the University of Washington School of Medicine, Seattle, WA, who is looking forward to assisting with research studies on WAGR syndrome during the summer of 2012.

Dr. Joan Han, pediatric endocrinologist, has been studying WAGR Syndrome at the National Institutes of Health in Bethesda, Maryland since 2006.

IWSA Members Attend Genetic Summit

In early March Kelly Trout and Shari Krantz attended the "Genetic Testing and Data Management Summit: Improving Health Outcomes, Disease Management, and Accountable Care Delivery" in Washington, DC. Hosted by the Genetic Alliance, Kelly and Shari joined a group of more than 150 individuals involved and interested in the rapidly growing field of genetics in medicine. Attendees represented a wide range of professions related to genetics, including policy makers, lab equipment manufacturers, researchers, physicians, healthcare/insurance organizations, genetic counselors, patient advocacy groups, and government agencies.

Discussions during the day facilitated interesting exchanges about the state of affairs in genetic testing, current and future trends in diagnostic technologies, information utility, and the regulatory environment. Various panels explored patient-oriented strategies, clinician-focused approaches, and developing both short- and long-term recommendations to enhance the optimal delivery of genetic-related services to patients. Overwhelming amounts of genetic information is entering the healthcare system from the scientific and testing communities and there are many issues as a result. Reimbursement for genetic testing and counseling, better support and training for clinicians, and limited training in the use of genetic technologies were also explored and debated.

With IWSA support and travel scholarship assistance from the Genetic Alliance, Kelly was able to travel from her home in San Antonio, Texas to Washington, DC to attend the Summit. Kelly serves the IWSA as our Medical Advisor and also as a Board Member. Shari lives in a Maryland suburb of Washington, DC and serves as an IWSA Board Member. The Summit provided a great opportunity for Shari and Kelly to represent the IWSA as a small, rare disease nonprofit group--devoted to WAGR/11p Deletion families--and to learn more about genetics and how they relate to the health and care of WAGR individuals.

WAGR Weekend 2012
July 20th-22nd

Gaithersburg, Maryland

Hosted by the Krantz/Marshall Family

SpringHill Suites by Marriott

9715 Washingtonian Blvd.

(301) 987-0900

Special Room rate $69.99/night for

2 Double beds—Limited Rooms Available

Saturday Activities will be held at

Bohrer Park Activity Center

508 S. Frederick Ave.

Gaithersburg, MD 20877

Financial Assistance is Available
Contact Tammie Hefty
tammiehefty@yahoo.com
(all requests are confidential)

Please join us for a wonderful weekend

Aniridia Network
UK Conference 2012

When: 19th May 2012 - timings (roughly) 10am - 4pm with social activity to follow (optional)

Where: Manchester Conference Centre, Manchester

Prices: £15 adults (18 and over), £7.50 13-17 year olds and children (12 and under) free

Please contact Jenny Langley at jcl_27982@hotmail.com with any questions

IWSA
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On behalf of all our families, the IWSA Board and Officers, would like to thank everyone that has made monetary donations to our great cause. We could not carry out our mission without your support.

Volunteers Needed for Meal Studies during WAGR Weekend

Researchers at the National Institutes of Health are inviting children and adults with WAGR/11p deletion syndrome, age six years and older, to participate in meal studies. This study will be conducted in conjunction with WAGR Weekend 2012, on the morning before (Friday, July 20, 2012) or the morning after (Monday, July 23, 2012). Prior WAGR studies research participants and new participants are all welcome. This study involves spending one morning at the NIH Clinical Research Center in Bethesda, Maryland (about 10 miles from the hotel site of WAGR Weekend). This specific study will include drinking a breakfast shake at 8 AM and eating a chicken nuggets lunch at noon. Entertainment (games, crafts, movies, and other light activities) will be provided between breakfast and lunch. The purpose of this study is to learn about satiation and satiety using single-item meals adapted for people who have visual impairment.

A blood draw is not necessary, except for those who have not had prior genetic testing at the NIH.

For more information, please contact Amanda Huey at WAGR_Study@mail.nih.gov or 301-451-7163.

International WAGR Syndrome Association
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