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eXtraOrdinarY Kids

Research Newsletter

**Children's Hospital Colorado,
University of Colorado Anschutz Medical Campus**



From the desk of Dr. T

Dear Friends and Supporters of the *eXtraordinary Kids Clinic* and Research Program,

Welcome to our first research newsletter! When my research on XYY syndrome started in 2004, I never imagined that the project would expand and build into the fantastic program we have today that includes all X&Y variations. Thanks to a dedicated research team and support from various granting agencies and Children's Hospital Colorado. But, most importantly, our projects and successes should be credited to the parents, kids, teens, and adults who have participated in our research projects. You all are the ones who continue to bring up important research questions that guide our projects, and also who have dedicated your time and efforts participating in studies. The experience of X&Y chromosome disorder families continues to inspire our work, and we want to share with you updates and accomplishments so you all can see how your contributions make a difference and lead to important results. The research process can be slow sometimes, with all the regulations, paperwork, and time it takes to collect and publish data. However, step-by-step, I truly believe we are making progress toward improving the lives and medical care for individuals and families with these conditions, and we're not stopping! Enjoy learning about our projects!

D. TARTAGLIA MD

Special points of interest:

- eXtraordinary Babies Study is still recruiting babies! We especially are looking for infants with 47,XXX & 47,XYY.
- New clinic registry for all X & Y Variations!
- Summer research expo prepares trainees at Children's Hospital of Colorado for research in X & Y variations.
- Clinical research uncovers interesting new medical findings!

Letters from Research Participants

"Just wanted to thank the team for an incredible visit to Denver last week. Our son had such a blast and it was wonderful to know that we have a team of great people who are just as invested in his well-being as we are. We can't wait until next year!"

"It meant a lot to come out here and to have someone like you take care of us... Much appreciated!"

"My family is so thankful for your team and all the effort you are putting into learning more about XYY and children with X & Y variations."

Understanding Early Development

Research in birth-to-age five children



Natural History of Sex Chromosome Aneuploidies

The *eXtraordinary Babies Study* is underway and in full swing! This natural history study will answer many of our questions about the medical, hormonal, and developmental features associated with prenatally diagnosed X&Y chromosome trisomies. **Participation in this study helps to provide accurate information to doctors and genetic counselors about X&Y chromosome variations, and will allow us to be able to more accurately answer questions about the early factors that may predict later learning or emotional difficulties, so that interventions can be started earlier.**

We have 2 active study sites:

- *Children's Hospital Colorado*
- *Nemours/DuPont Hospital in Delaware (Site-PI Judy Ross, MD)*

The study covers *reasonable travel expenses* for families to get to their nearest and most convenient site.

We are making great progress toward our enrollment goals. However, in order to best represent the full population of children with X&Y variations, we are focusing our recruitment in the next year on children age **6-12-months** with **prenatally identified: 47,XYY, 47,XXX, & 48,XXYY**. Infants with 47,XYY will continue to be enrolled until we meet our final goal.

Thank you so much to the families participating in this important research. Please share our contact information with any families you think might be interested!

	Enrolled	Goal
Total	132	200
XXY	95	100
XYY	13	50
XXX	21	50
XXYY	3	N/A

Growing up with Trisomy of the X&Y Chromosomes: the TRIXY study

This study is led by the esteemed **Sophie van Rijn, PhD** (pictured) in the Netherlands. We were so proud to be selected as a collaborating US site. TRIXY is designed to learn more about early predictors for future outcomes of learning, behavior, and social skills in young children with X&Y variations. When this is better understood, interventions can be developed to improve social-emotional functioning from a young age. We have successfully enrolled 60 participants at our site in this international collaboration. Follow-up visits will continue through Sept. 2020. Preliminary results on the baseline visits of the study were presented by Dr. van Rijn at the AXYS Conference in Atlanta, GA. Publications are forthcoming in late 2020 – early 2021. See preliminary results at: www.genetic.org/about/conference-mtrls/2019-axys-family-conference-atlanta-georgia/



Participant Hometowns

Families travel from all across the country (and Canada!) to participate in our research studies.

We know how much work it is to travel with very young children. Thank you for making the effort to get here for each visit!

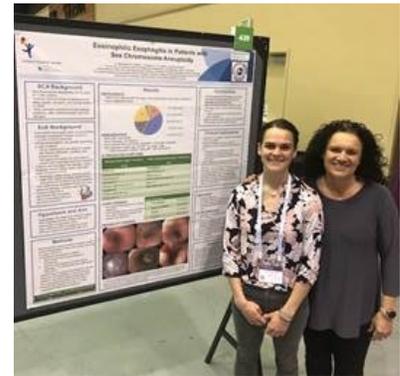
Preparing Future Researchers in X & Y Conditions

eXtraOrdinarY Kids Training Program

Relationship Between EoE and X&Y Variations

In our *eXtraOrdinarY Kids Clinic* we have observed that some children with extra X and/or Y chromosomes also have a diagnosis called Eosinophilic Esophagitis (EoE). EoE is a rare immune-mediated disease in the esophagus—the tube that connects the mouth down to the stomach.

We went back to our records for the patients seen in clinic and found ~3% had a biopsy-confirmed diagnosis of EoE—that is 60 times higher than in kids without X&Y variations!! One of our genetic counseling graduate students, Catherine Buchanan, under mentorship of Susan Howell, presented this data at the American College of Medical Genetics (ACMG) meeting in Seattle, WA in April 2019 to help increase awareness of a possible relationship between X & Y variations and EoE. Check out the symptoms of EoE in the box and discuss with your child's doctor if several symptoms are present.



Symptoms of EoE

- Feeding difficulties
- Failure to thrive (poor growth)
- Reflux or regurgitation
- Difficulty swallowing food
- Food getting stuck
- Heart burn or chest pain
- Chronic abdominal pain
- Food allergies

eXtraOrdinarY Kids Research Expo 2019

A major part of our mission is to train future professionals across all disciplines in X & Y variations. Every year we welcome trainees of all levels on our clinic and research teams. This summer we hosted the first annual eXtraOrdinarY Kids Research Expo at Children's Hospital Colorado, organized by Dr. Shanlee Davis.

Eight trainees shared the results of current X&Y research on topics such as adaptive behaviors, parenting stress, population health, mitochondrial and vascular functioning, and educational supports and outcomes for students with X&Y variations. We are so proud to support new and innovative researchers in this field! Be on the lookout for future publications sharing these data and plan to join us next summer for the next research expo!



Advances in Turner Syndrome

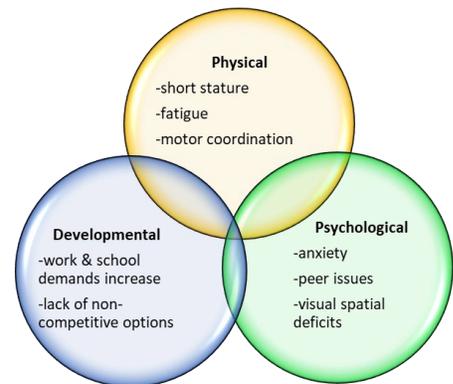
eXtraOrdinary Kids Clinical Research

Physical Activity for Teens with Turner Syndrome

Dr. Shanlee Davis and our team recently studied physical activity levels in 21 adolescents and young women with Turner syndrome.

Major findings:

1. Our sample was significantly less physically active than the general population.
2. Barriers to exercise include physical and psychological issues related to TS as well as unique developmental issues that arise in adolescence (See figure)
3. Structured and social fitness options may encourage more movement



Ideas for a more active lifestyle in adolescence:

- Play organized recreational sports with regular practice schedules
- Volunteer or work in an active environment (coach a young kids team, help out in a childcare setting, work at a local park or rec center)
- Assign active and social chores (daily dog walking with a sibling, rake leaves as a family)
- Participate with a friend in walking/running fundraisers for a favorite charity
- Park further away from your destination than necessary and chat with your daughter as you walk the extra blocks (or mile!)

Be on the lookout for a future publication with a more comprehensive list of recommendations for families, medical providers, educators, and therapists.

On the Horizon



◇ The eXtraOrdinary Kids Turner Syndrome Clinic, led by **Dr. Shanlee Davis**, has been chosen by the Turner Syndrome Global Alliance to lead a **national clinic registry** for girls with Turner syndrome! Our team will be working with other clinics around the country to develop a database that will track important outcomes from hundreds of patients over time. This project will allow us to answer questions we have not had the numbers for before. We are hoping to add other X&Y variations in the future – let us know if you would like to help support this project!

- ◇ Lots of new research findings will be published in 2020 about XYY, XXYY, Trisomy X, XXXY and XXY in a special edition of the *American Journal of Medical Genetics* dedicated entirely to X&Y chromosome variations. Dr. T will be a guest editor of this special edition, which will include over 20 papers by our team and others in the US and internationally that will be a comprehensive update of new research. After publication, we will summarize the important findings for families in another edition of the newsletter.

Hot off the Press!

Some of our most recently completed studies

Testosterone and Infant Boys with XXY

20 infant boys with XXY participated in a pilot study to look at the effects of early testosterone on fat and muscle. This led to the NIH funding a larger study, called TESTO, which is **currently enrolling boys with XXY 1-3 months of age**. Thanks to the families who have made this important study possible! Read the abstract here:

<https://academic.oup.com/jes/advance-article/doi/10.1210/js.2019-00274/5573707>



“Playing sports (or other organized physical activity) was related to better exercise capacity”

XXY Cardiometabolic Study

Does exercise seem harder for your child with XXY?

We recently studied 30 adolescents with XXY and found exercise capacity (or one's ability to perform physical activity) is 20% lower than adolescent males of similar age and BMI. These results mean that exercise is indeed harder for boys with XXY. We also saw that boys with XXY had higher percent body fat even though they were not obese, and that higher body fat was related to lower exercise capacity. But, playing sports (or other organized physical activity) was related to *better* exercise capacity – **so it is possible that poor exercise capacity can actually be prevented or improved with more exercise!** Thank you so much to all the boys who participated in this study. We plan to do more work in this area to better understand the underlying problem and determine if any other interventions can help.



Testosterone Effects in Adolescent Boys with XXY/Klinefelter syndrome

During early puberty, there is much variability in how and when doctors start testosterone therapy. Parents always ask, and doctors need to know, what aspects of XXY may improve with testosterone therapy, and which may be unrelated to testosterone treatment. This study evaluated the effects of testosterone gel therapy compared to placebo gel on behavior, mood, problem solving, attention span, motor skills, growth, and physical health in adolescent males with XXY in early puberty. We had 48 participants complete a 12-month study!

One question we have looked at, led by Richard Boada PhD and Caroline Harrison MPH, was whether testosterone led to improvements in attention or executive functioning (EF). EF describes brain functions such as organization, planning, working memory, initiation of tasks, shifting strategies when needed, and inhibition of impulses. Results showed that there was not a significant improvement in attention or EF in the group treated with testosterone compared to the placebo treatment.

Dr. T's conclusion from these results: While testosterone may have other benefits, it isn't an effective treatment for attention or EF problems in XXY in early puberty. Problems with attention or executive function in teens with XXY should be further evaluated by a psychologist so an individualized treatment plan can be developed, with consideration of medication treatment for ADHD in some cases. If physicians recommend that a young man with XXY be started on testosterone (by an endocrinologist) and an ADHD medication (by a pediatrician, developmental pediatrician or psychiatrist), then I recommend waiting a couple months between starting the two medications, since otherwise it is difficult to determine which medication may be contributing if side effects occur. Stay tuned for more results from this study and THANK YOU to all the families that hung in there for this long but important study!

eXtraOrdinarY Kids Clinic

The eXtraOrdinarY Kids Clinic was launched in 2007 by Founder and Director Nicole Tartaglia, MD in order to provide **Comprehensive Care**, **Dedicated Advocacy**, and **Essential Research** for children and adolescents with X & Y variations.

Here are some ways you can support our program:

	Participate <ul style="list-style-type: none">• Go to our website to see if you are eligible for any current research studies• www.extraordinarykidsclinic.org
	Spread the word <ul style="list-style-type: none">• Share this newsletter or our contact information with your social networks!
	Donate <ul style="list-style-type: none">• Tax deductible!• Go to: childrenscoloradofoundation.org/extraordinarykidsclinic

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And, MOST OF ALL, thank you to the eXtraOrdinarY Kids and Families who participated!

