Washington University School of Medicine
Wolfram Research Clinic Newsletter
May 1, 2016 Vol.3

WU Wolfram Research Clinic

WU Wolfram Research Clinic

Dear Patients and Families,

As the 2016 Wolfram Research Clinic gets closer it may be helpful to know what to expect between now and then. Here is a timeline of what's to come:

ASAP – All patients, new and returning, need to be sure that we have all records of any hearing, vision, imaging and/or sleep testing that the patient has had done on file. The doctors at the clinic use these records to create a comprehensive evaluation for the patient so it's critical that we have these in time to share them with them prior to the clinic. If you need a release of information from WU to give to your physician please contact Samantha.

May 2016 – ACTION ITEM! Consent forms and bladder diaries will be sent out. This is an action item as you'll be asked to complete these forms and return them to us right away.

Early June 2016 - ACTION ITEM! Once we receive the signed consent forms we will then send the on-line survey for both the parent (proxy) and the patient to complete. **This survey must be completed prior to 7/4/16.**

* Samantha Ranck, Research Clinic Coordinator *
rancks@npg.wustl.edu or **314-362-6514**

ENROLLMENT

Enrollment for this year's clinic is now closed. However, if you or anyone you know is interested in more information regarding future clinics please ask them to contact Samantha.

REMINDERS

The 2016 clinic will be held from the evening of **Tues., 7/12/16 thru Sat., 7/16/16.** There are opportunities to begin testing earlier in the week so if you are interested in coming early please contact Samantha right away so that the appropriate arrangements can be made.

RESEARCH UPDATE

WU welcomes Dr. Timothy Barrett!

Since the last newsletter, **we have made significant progress towards pooling information across Wolfram clinic sites in the US and Europe.** We were excited to host Dr. Timothy Barrett from the University of Birmingham, UK, at WU in early April to take part in our Pediatric Diabetes Research Consortium Symposium (pdrc.wustl.edu). Dr. Barrett gave the keynote speech on his experiences with Wolfram Syndrome, and I followed to give an update on our Wolfram Research Clinic. The next day, Dr. Barrett met with us to discuss how best to collaborate going forward.

It was an extremely productive visit. We were able to agree on measures that both sites could perform. In addition, we had Dr. Barrett undergo the same MRI scan that people with Wolfram Syndrome do at our Research Clinic! On his return home, he will be scanned again on the UK scanner, so that we can compare images. All of this work will go into our grant proposal to the National Institutes of Health. We hope to convince them to fund research efforts at both clinics and possibly at two sites in France.

Importantly, we also discussed the best way to incorporate measures from the research clinic into future clinical trials, to maximize our ability to determine any drug's effectiveness. We will see Dr. Barrett and the rest of the Wolfram research community in June at the International Wolfram Syndrome meeting, and will update you with their progress at the next clinic. We are looking forward to seeing all of you soon in St. Louis!

Best,

Tamara Hershey, PhD (tammy@wustl.edu)
Professor & Scientific Director of Research Clinic

For more information about Wolfram Syndrome or the Wolfram Syndrome Research Clinic please visit:
hersheylab.wustl.edu

CLINICAL CARE UPDATE

Wolfram Syndrome vs. WFS1-related disorders: It is all in the name

Best wishes to all the Wolfram families! As Dr. Hershey mentioned, Dr. Timothy Barrett visited Washington University this past April. In addition to giving an outstanding talk, Dr. Barrett discussed the variability in symptoms that people with "Wolfram Syndrome" can have. ***We agreed that the term "Wolfram Syndrome" can be misleading since it implies that everyone will have the same set of symptoms and will progress in the same way.***

This confusion arose for the following reason: Before the *WFS1* gene was identified by Dr. Permutt in 1989, and testing for the gene mutations was possible, the only way to diagnose "Wolfram Syndrome" was by identifying a certain set of symptoms – optic atrophy, diabetes, mellitus, diabetes insipidus and deafness. This approach meant that ***only people with these most noticeable symptoms were diagnosed with Wolfram Syndrome***. Papers from that time describe these severe symptoms and their progression as a necessary part of the disease.

However, now that we can test for *WFS1* gene mutations, we find that many people who are genetically-diagnosed with Wolfram Syndrome don't necessarily look like our original picture of clinically-diagnosed Wolfram Syndrome. In other words, we now see a much wider range of symptoms, severity and rate of progression in people with *WFS1* mutations compared to our previous definition of Wolfram Syndrome. Some people with WFS1 mutations may experience minimal symptoms while others may experience more severe or widespread symptoms; some may have later development of these symptoms or may never have them at all. In the past, these people may not have received a diagnosis of "Wolfram Syndrome" because they didn't fit the definition that was used.

Based on findings from the WU Wolfram Research Clinic, Dr. Barrett's clinical experience and reports from across the world, we now have much broader knowledge of *WFS1* mutation-related symptoms. In addition, better medical care and earlier diagnosis may be contributing to longer lifespans for all affected people. ***Thus, we urge families to remember that what they see in older papers or on the web may not always be relevant to their loved one with WFS1 mutations.***

We and others are actively exploring how different types of *WFS1* mutations may relate to different symptoms. In addition, at the 6th International Wolfram Workshop in June, Dr. Barrett will be leading a discussion of how to better understand the range of symptoms associated with *WFS1* mutations. ***This discussion could lead to new naming conventions and a move away from using the term "Wolfram Syndrome" for every type of WFS1 mutation.*** One possible outcome is the use of the term *WFS1*-related disorders. However, this topic awaits the input of all the Wolfram experts across the world. We will give you an update on this discussion after we return from the meeting in June, so please stay tuned!

Bess Marshall, MD
Pediatric Endocrinologist & Research Clinic Medical Director

High Praise!

An article based on data from the WU Wolfram Research Clinic was recently featured in the Orphanet Journal of Rare Disease's top 10 most influential articles of 2015!! This article describes the Wolfram Unified Rating Scale (WURS) a measure that captures individual differences in disease severity in children and young adults with WFS. If you would like a copy of the article sent to you please contact Samantha.

TITLE: Reliability and validity of the Wolfram Unified Rating Scale (WURS)
AUTHORS: Nguyen, Foster, Paciorkowski, Viehoever, Considine, Bondurant, Marshall, Hershey and the Washington University Wolfram Syndrome Research Study Group

Timothy Barrett MD, Tamara Hershey PhD, Neil White MD and Paul Hruz MD at the Pediatric Diabetes Research Consortium Symposium at WU in April of 2016.