

# University of Rochester Batten Center

## Newsletter

### Summer 2015

#### University of Rochester Batten Center (URBC) Updates

- ❖ *We will be collaborating with researchers at Massachusetts General Hospital to better understand multiple forms of Batten disease.*
- ❖ *We are recruiting children and adults **with all forms of Batten disease** to take part in the natural history study.*
- ❖ *We are running a new study for parents of children with JNCL that involves answering a series of questions online.*

#### Telemedicine-What is it and how can it help me?

##### What is telemedicine?

Telemedicine is the use of electronic communication to exchange medical information remotely between a health care provider and a patient.

##### What services can be provided?

- Primary care and specialist referral services
- Remote patient monitoring
- Consumer medical and health information
- Medical education

##### What are the benefits to you?

- Telemedicine allows patients to receive care from specialists who are located far away without having to travel to visit them.
- Telemedicine can benefit patients living in remote regions by improving access to care.
- Traveling long distances is a barrier for many families who are otherwise interested in participating in research studies. Telemedicine can decrease or eliminate travel, allowing more families the opportunity to participate in research studies that take place in other parts of the country.

The URBC has conducted research related to telemedicine. We found that that the Unified Batten Disease Rating Scale (UBDRS) is reliable and feasible for remote administration. Preliminary data also suggest that remote cognitive assessment may be feasible and reliable in children with JNCL.

#### Educational Services for Your Child with Batten Disease

Educational services for a child with Batten disease can range from informal arrangements with individual teachers, to formal supports and accommodations provided by a Section 504 Plan or an Individualized Education Plan (IEP). Both the Section 504 Plan and the IEP arise from federal laws that address the needs of individuals with disabilities. A 504 Plan or IEP can change at any time if the child's needs change.

**Section 504 Plan:** A Section 504 Plan is so-named after Section 504 of the Rehabilitation Act of 1973, which prevents discrimination, by programs receiving federal funding, against individuals with disabilities. For students in grade school, the goal of a 504 Plan is to level the playing field, providing equal access to the educational setting alongside non-disabled peers. 504 Plans are appropriate when a student has a disability that limits his or her life in one or more ways, though the limitations don't have to be school-specific. For example, some children with early-stage juvenile Batten disease may benefit from services to address vision loss, and if provided, can still participate in the regular education setting.

**Individualized Education Plan (IEP):** An IEP is appropriate for students who experience an educational impact of their disability. Most children with Batten disease will eventually benefit from IEP services, due to the educational impact of their disability. An IEP is set up by the school district's Committee on Special Education (CSE). Like 504 Plans, the IEP provides support, services, and accommodations, but recognizes a higher level of need. The IEP also recognizes the need for modifications such as an adapted curriculum, so your child can participate to the best of his or her own personal ability level. The CSE will require periodic reassessment (such as academic testing). At a minimum, this happens every 3 years. However, children with Batten disease may need more frequent re-testing, since learning needs can change from year to year.

The first step in getting a 504 Plan or IEP for your child is to contact the school district's Special Education department, who can walk you through the process. Dr. Adams, the URBC Neuropsychologist, is glad to address any questions that parents or schools may have about special education services. Also, the BDSRA's Family Support Officer, Becky Hetteberg, is available to assist. The BDSRA also has excellent online resources at: <http://bdsra.org/patient-and-family-support/educational-resources/>

# Research

## New Collaboration

We are excited to report that the URBC will be expanding its research to focus on the natural history of INCL and LINCL. The URBC and Massachusetts General Hospital (MGH) have joined forces to combine the natural history research expertise at URBC with the molecular diagnostic and biorepository expertise at MGH. This collaboration creates the opportunity to advance knowledge about the natural history and disease biology of CLN1 (Infantile; INCL) and CLN2 (Late Infantile; LINCL). Currently, little is known about the way different genetic mutations in INCL and LINCL affect the observable characteristics of the disease. We seek to better understand the connection between these factors. Although this is a new scientific collaboration, UR and MGH have a long history of working together as experts in Batten Disease and in Child Neurology more broadly. Dr. Katherine Sims (MGH) and Dr. Jonathan Mink are each directors of BDSRA Batten Disease Centers of Excellence. They have a strong working relationship and look forward to advancing knowledge about CLN1 and CLN2 that would not be possible without working in parallel.

## Function and Quality of Life in JNCL

The University of Rochester Medical Center is currently recruiting parents of individuals with genetically confirmed (CLN3) Juvenile Neuronal Ceroid Lipofuscinosis (JNCL) for a research study. The purpose of this study is to learn how to measure changes in function and quality of life of people with JNCL, using parent questionnaires. The study will last a minimum of 18 months and up to 24 months. It involves completing a series of four online surveys once every six months. You must be a parent of an individual with genetically confirmed JNCL, able to speak English, and have access to a computer, internet, and a current email address. You will be paid with a \$25 gift card for each complete set of questionnaires, up to \$125 for completion of 5 assessments over 24 months. There will be no cost to you to participate. To learn more about this study, you can click on the following website link: <https://redcap.urmc.rochester.edu/redcap/surveys/> and enter the code: WEJTCHE8P. This link will also allow you to enroll in the study if you choose to participate. If you have any questions about the study, please contact Sara Defendorf (Study Coordinator) or Dr. Erika Augustine (Principal Investigator) at (585) 273-3810 or by email at [Batten@urmc.rochester.edu](mailto:Batten@urmc.rochester.edu).

## Natural History Research

We developed the Unified Batten Disease Rating Scale (UBDRS) to provide a consistent and disease-specific approach to evaluating individuals with JNCL. The UBDRS has two main parts: a physical exam and an interview about medical history and symptoms of Batten Disease (such as seizures). The UBDRS is used in two ways – as part of a clinical evaluation at the URBC and as a research tool.

Using the UBDRS, we track disease progression over time. This has enabled us to describe the natural history of JNCL, including the symptoms that lead to disability, and potential factors that are related to fewer symptoms or lesser disability. We are now expanding our research to include other forms of Batten disease. Since 2002, 130 children and adults with Batten disease have taken part in this study, and many return each year!

**We invite families to participate in this study.** Study visits take place in Rochester, NY at the URBC and/or at annual Batten Disease Support and Research Association meetings. For more information about participating in our natural history study, contact Amy Vierhile at (585) 275-4762 or email us at: [batten@urmc.rochester.edu](mailto:batten@urmc.rochester.edu).

## Participation in FDA Workshop

Dr. Mink and Dr. Adams recently participated in a two-day workshop (April 16-17, 2015) at the U.S. Food and Drug Administration, “Public Workshop on Assessment of Neurocognitive Outcomes in Inborn Errors of Metabolism and Advancing the Development of Pediatric Therapeutics (ADEPT)”. The first day of the workshop focused on assessing neurocognition, as an efficacy outcome, in clinical trials for individuals with disorders such as Batten disease. The second day of the workshop focused more generally on assessment of neurocognition in the developing child. Dr. Mink presented two talks on Day 1: “*Clinician Perspective*” (focusing on clinician perspectives related to efficacy clinical trials, and “*Batten Clinical Rating Scale*”, an overview of the UBDRS. Dr. Adams presented a talk on Day 1 of the workshop, “*Use of remote technology to expand the reach of clinical research*”. This talk reviewed the URBC’s work to evaluate children with Batten disease through remote, live video visits. Full details of the workshop, including all slide presentations, are publicly available at the FDA website: <http://www.fda.gov/Drugs/NewsEvents/ucm434954.htm> and a transcript of the meeting is forthcoming.

# Selected Publications



From left to right: Heather Adams, PhD; Elisabeth de Bleeck, MPA, CCRC; Sara Defendorf, BS, CCRP (back); Jonathan Mink, MD, PhD; Frederick Marshall, MD; Amy Vierhile, RN, PNP; Alyssa Thatcher, BS; Paul Rothberg, PhD; Erika Augustine, MD

**Adams HR; Rose K; Augustine EF; Kwon JM, de Bleeck EA; Marshall FJ; Vierhile A; Mink JW; Nance MA. Experience, knowledge, and opinions about childhood genetic testing in Batten disease. *Molecular genetics and metabolism*. 2014; 111(2): 197-202.**

This study sought to understand parents' perspectives, knowledge, and experiences related to genetic testing for Batten disease. The majority of parents felt it was better to know ahead of time that a child would develop Batten disease, believed that this knowledge would not alter how they related to their child, and that parents should have the final say in deciding whether to obtain genetic testing in children. Participation in any genetic counseling was associated with greater knowledge on questions about genetics.

**Mink JW, Augustine EF, Adams HR, Marshall FJ, and Kwon JM. Classification and Natural History of the Neuronal Ceroid Lipofuscinoses. *J Child Neurol* 28: 1101-1105, 2013.**

There are several forms of Batten disease that vary in age of onset, specific neurologic phenotype, and rate of progression. We describe 9 major forms and present a classification scheme. Understanding the age of onset, clinical features, and natural history can inform rational diagnostics. Better knowledge of the natural histories of these disorders is necessary to shed light on the underlying pathobiology and to develop new therapies.

**de Bleeck EA; Augustine EF; Marshall FJ; Adams H; Cialone J; Dure L; Kwon JM; Newhouse N; Rose K; Rothberg PG; Vierhile A; Mink JW. Methodology of clinical research in rare diseases: Development of a research program in juvenile neuronal ceroid lipofuscinosis (JNCL) via creation of a patient registry and collaboration with patient advocates. *Contemporary Clinical Trials* 2013; 35:48-54.**

This publication describes ways in which we have been able to carry out studies related to Batten disease. We created a registry where families can elect to enroll if they wish to be contacted about research studies. Currently, 198 families are enrolled, representing 237 children with Batten disease. Furthermore, the BDSRA has referred participants, and the annual BDSRA meetings have allowed us to enroll participants and complete studies.

**Cialone J; Adams H; Augustine EF; Marshall FJ; Kwon JM; Newhouse N; Vierhile A; Levy E; Dure LS; Rose KR; Ramirez-Montealegre D; de Bleeck EA; Mink JW. Females experience a more severe disease course in Batten disease. *J Inherit Metab Dis*. 2012; 35:549-55. (Erratum in *J Inherit Metab Dis*. 2012; 35:559).**

We investigated differences between males and females with JNCL. Using data from the UBDRS, the BDSRA database, and a quality of life questionnaire (PedsQL), we found that JNCL symptoms began, on average, one year later in females than in males. Furthermore, female age at death was one year earlier than males. Overall, affected females had lower functional abilities, earlier loss of independent function, and lower physical quality of life than males.

**Cialone J; Augustine EF; Newhouse N; Vierhile A; Marshall FJ; Mink JW. Quantitative telemedicine ratings in Batten disease: implications for rare disease research. *Neurology*. 2011; 77:1808-11.**

The purpose of this study was to determine if the Physical Impairment section of the UBDRS could be feasibly and reliably administered remotely using live video. Two trained raters scored the same exams using live video. The UBDRS Physical Impairment section is reliable when administered with telemedicine methods.

**Kwon JM; Adams H; Rothberg PG; Augustine EF; Marshall FJ; DeBleeck EA; Vierhile A; Beck CA; Newhouse NJ; Cialone J; Levy E; Ramirez-Montealegre D; Dure LS; Rose KR; Mink JW. Quantifying physical decline in juvenile neuronal ceroid lipofuscinosis (Batten disease). *Neurology*. 2011; 77:1801-7.**

In this study, the UBDRS was used to measure the rate of physical and functional decline in individuals with JNCL. Physical impairment and functional capability worsened over time at an even rate following the initial symptom onset. The rate of decline did not depend on specific types of CLN3 mutations. The UBDRS is a reliable and valid instrument that measures symptom progression in JNCL.

**Cialone J; Augustine EF; Newhouse N; Adams H; Vierhile A; Marshall FJ; de Bleeck EA; Kwon J; Rothberg PG; Mink JW. Parent-reported benefits of flupirtine in juvenile neuronal ceroid lipofuscinosis (Batten disease; CLN3) are not supported by quantitative data. *J Inherit Metab Dis*. 2011; 34:1075-81.**

We used the UBDRS to investigate the impact of flupirtine on disease progression in JNCL. The age of loss of independent walking, understandable speech, and the ability to perform independent activities of daily living was examined. Although many families perceived flupirtine to be helpful, our data showed that flupirtine had no effect on disease progression.



# Selected Publications

**Adams HR; Beck CA; Levy E; Jordan R; Kwon JM; Marshall FJ; Vierhile A; Augustine EF; DE Blieck EA; Pearce DA; Mink JW. Genotype does not predict severity of behavioural phenotype in juvenile neuronal ceroid lipofuscinosis (Batten disease). Devel Med Child Neurol. 2010; 52:637-43.**

In this study we asked if the specific JNCL genetic mutation (called "genotype") affected a child's everyday clinical symptoms (called "phenotype"). About 85% of children have the same 'common' genotype pattern. We compared a group of children with the common genotype to children with different JNCL-causing mutations. We did not find any relationship between "genotype" and "phenotype", meaning that behavioral symptoms were similar in the two groups. The genotype (JNCL mutation) did not seem to influence the severity of a child's behavioral symptoms.

**Adams HR; Kwon J; Marshall FJ; de Blieck EA; Pearce DA; Mink JW. Neuropsychological symptoms of juvenile-onset Batten disease: experiences from 2 studies. J Child Neurol. 2007; 22:621-7.**

This paper describes two studies of cognitive skills in children with juvenile Batten Disease. 1. 15 children with JNCL completed a brief test of their ability to pay attention. Their attention performances were lower than expected for their age, when compared to non-Batten affected groups. 2. 18 children with Batten disease completed more detailed cognitive testing. Compared to healthy, same-age peers, their scores were significantly lower on tests of attention, memory, verbal fluency, and general verbal reasoning skills. There were no significant differences between males and females. Cognitive skills were lower among children with a history of seizures. However, this study cannot tell us if seizures contributed to worse cognitive performance, or if some other factor influenced both seizures and cognitive skills.

**Adams H; de Blieck EA; Mink JW; Marshall FJ; Kwon J; Dure L; Rothberg PG; Ramirez-Montealegre D; Pearce DA. Standardized assessment of behavior and adaptive living skills in juvenile neuronal ceroid lipofuscinosis. Devel Med Child Neurol. 2006; 48:259-64.**

We examined behavior and adaptive living skills in children and young adults with Juvenile Batten Disease (JNCL). We found that behavioral and psychiatric symptoms were both frequent and severe in more than half of the study participants. The frequency of these problems did not differ in males and females. Compared to healthy same-age peers, children with JNCL had limitations in their adaptive living skills, such as self-care, hygiene, socialization, and other age-expected, everyday tasks.

**Kwon JM; Rothberg PG; Leman AR; Weimer JM; Mink JW; Pearce DA. Novel CLN3 mutation predicted to cause complete loss of protein function does not modify the classical JNCL phenotype. Neurosci Lett. 2005; 387:111-4.**

Much can be learned about the function of a protein and how it causes disease by analyzing the effects of mutations. This paper reports a case of JNCL with a unique mutation that causes a stop signal very close to the beginning of the CLN3 protein. The patient had a clinical course that did not differ from JNCL patients with other mutations.

**Marshall FJ; de Blieck EA; Mink JW; Dure L; Adams H; Messing S; Rothberg PG; Levy E; McDonough T; DeYoung J; Wang M; Ramirez-Montealegre D; Kwon JM; Pearce DA. A clinical rating scale for Batten disease: Reliable and relevant for clinical trials. Neurology. 2005; 65:275-9.**

We developed the UBDRS clinical rating scale to assess the physical-, seizure-, and behavior-related impairment and the functional abilities of individuals with JNCL. We found that the UBDRS is a reliable instrument that can be used to effectively monitor symptoms in individuals with Batten disease.

**We thank all of the children and families who participate in our research.**

**You make it possible for us to do this work!**

## Participate in a Research Study

We will be attending the 2015 Batten Disease Support and Research Association (BDSRA) National Conference, and we look forward to seeing you there! This year's conference, planned by the staff of the BDSRA and the Midwest Chapter of the BDSRA, will be headquartered at the Eaglewood Spa and Resort in Itasca, IL from July 9<sup>th</sup>-July 12<sup>th</sup>. Online conference registration can be accessed at [www.bdsra.org](http://www.bdsra.org). For questions, please call Tracy Kirby at 800-448-4570.



***We love to hear from you! Please contact us with your questions and comments.***

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