



Cystinosis Research Network 2021 Virtual Family Conference

July 16-18, 2021 (all times Eastern Daylight Time)

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Friday, July 16th

6:00 pm – 8:00 pm **Conference Kickoff/Family Introductions**

*Hosts: Jonathan Dicks, VP Development and Jen Wyman, VP Family Support
Please join us for welcome and overview of the conference and family introductions. Bring your entire family!*

Saturday, July 17th

10:00 – 10:30 am **Welcome and CRN Overview**

Tim Wyman, President, Christy Greeley, VP Research, Executive Director

10:30 am – 11:00 am **Cystinosis – A Review of Old and New**

J.J. Zaritsky, MD, PhD

A review of the epidemiology, pathophysiology and treatment options of Cystinosis.

11:00 am – 11:30 am **Anticipating Renal Replacement Therapy/Stanford protocol combined stem cell transplant and kidney transplant from same living donor**

Paul Grimm, MD

Unfortunately, even when children are diagnosed with cystinosis at a young age and they are able to tolerate the cystine depleting therapy, there may be substantial damage already done to the kidneys. As the child grows, the kidneys may not have the reserve to grow with the child and even with excellent care the child or young adult may develop kidney failure. With this in mind, it is important to understand your kidney function. This presentation will empower you with a better understanding and ability to interpret the kidney function numbers of your loved one with cystinosis. This will be relevant to people at any stage in their disease journey, whether they are still using their original kidneys or have had their kidneys function replaced with the transplant. Near the end of the session I will introduce you to a new option for children and young adults who are approaching a kidney transplant and have a living donor. The opportunity to participate in a study of combined stem cell and kidney transplantation being offered at Stanford that could lead to freedom from taking cysteamine and freedom from immunosuppressive medications, potentially for the rest of your life.

11:30 am – 12:30 pm Panel Session 1

Panel Sessions are targeted towards different stages of the Cystinosis journey, divided into tracks by age. They will be smaller group sessions with a panel of experts presenting information, guiding discussion and fielding questions. Attendees should feel free to attend sessions of most interest to them.

Caregiver/Infant & Child (0-10): Cystinosis 101

Moderator: Jen Wyman, VP Family Support

Panelists: J.J. Zaritsky, MD, PhD Craig Langman, MD, Ranjan Dohil, MD Paul Goodyer, MD, Ewa Elenberg, MD, MEd, Rachel Bishop, MD

Teenager (11-17): Cystinosis 201

Moderator: Herberth Sigler, Board Member

Panelists: Rick Kaskel, MD, PhD, Larry Greenbaum, MD, PhD, Mihir Thacker, MD, Minnie Sarwal, MD, FRCP, DCH, PhD

Adult (18+): Cystinosis 301

Moderator: Marybeth Krummenacker, VP Education and Awareness

Panelists: Bill Gahl, MD, PhD, Galina Nesterova, MD, FABMG, Jess Thoene, MD Elena Levtchenko, MD, PhD, Roz Mannon, MD

12:30 pm – 1:00 pm Break

1:00 pm – 2:00 pm

Panel Session 2

Panel Sessions are targeted towards different stages of the Cystinosis journey, divided into tracks by age. They will be smaller group sessions with a panel of experts presenting information, guiding discussion and fielding questions. Attendees should feel free to attend sessions of most interest to them. Some sessions are closed as noted below.

Caregiver/Infant & Child (0-10): Neurocognitive & Educational Issues

Moderator: Jonathan Dicks, VP Development

Panelists: Doris Trauner, MD

A cognitive and behavioral profile has been found in children with cystinosis

- *Background of normal intelligence, language, and visual perceptual functions*
- *Difficulty with visual spatial skills, visual memory, motor coordination, and attention*
- *Academic difficulties—especially in math and spelling*
- *High incidence of behavioral problems and social difficulties*
- *Difficulty with executive functioning, including cognitive flexibility, behavioral regulation, shifting attention (can adversely affect disease management, adherence, and QOL)*

The brain appears to develop differently in children with cystinosis, correlating with visual spatial deficits

- *Volume loss, with enlarged ventricles, and reduced volume of cerebral cortex and white matter*
- *Delays in maturation of white matter fiber tracts in areas of the brain associated with visual spatial and visual memory functions (primarily parietal lobes)*
- *Reduced thickness of parietal lobe structures and delayed myelination in the parietal lobes compared to age-matched controls*

Teenager (11-17): Transplant and Dialysis

Moderator: Jenni Sexstone, Board Member

Panelists: Paul Grimm, MD, Rick Kaskel, MD, PhD, Roz Mannon, MD, Ewa Elenberg, MD, MEd Minnie Sarwal, MD, FRCP, DCH, PhD, Larry Greenbaum, MD, PhD

Adult (18+): Living with Cystinosis as an Adult: Healthcare, Expectations, Self-Management, Reproductive Issues, Mental Health Issues

(closed session for cystinosis adults and their partners)

Moderator: Sara Healy, Adult Leadership Advisory Board (ALAB) Member

Panelists: Maya Doyle, MSW, PhD, LCSW-R, Bill Gahl, MD, PhD, Galina Nesterova, MD, FABMG, Elena Levchenko, MD, PhD

Parents of Adults with Cystinosis

(closed session for parents of adults with cystinosis)

Moderator: Carol Hughes, Board Member

The purpose of the session is intended to be a private setting for parents of adults with cystinosis to share information, insight, advice and encouragement. This session will provide an opportunity to learn from others who face similar challenges, and allow you to talk about your experiences.

2:00 pm – 3:00 pm Medical Panel

Moderator: Bill Gahl, MD, PhD, Christy Greeley, VP Research, Executive Director

Panelists: Paul Grimm, MD, Craig Langman, MD, Jess Thoene, MD, Rick Kaskel, MD, PhD, Rachel Bishop, MD, Doris Trauner, MD, Larry Greenbaum, MD, PhD, Paul Goodyer, MD

Please join for the unique and informative opportunity to have your questions and concerns addressed by the leading physicians and researchers in Cystinosis. Questions will be gathered during the course of the conference utilizing the chat function.

Sunday, July 18th

10:00 am – 10:05 am Welcome

Christy Greeley, VP Research, Executive Director

10:05 am – 10:20 am Cystadrops® (cysteamine ophthalmic solution) 0.37%: distribution, resources, and support services for caregivers and adult patients *Helga Nematic, BSN, RN, CRA, National Patient Advocacy Liaison (PAL), Recordati Patient Support Services, Recordati Rare Diseases, Candace Gafford, Insurance Services, Anovo Specialty Pharmacy, Nelson Burford, Doctor of Pharmacy, Anovo Specialty Pharmacy*

Recordati Rare Diseases is pleased to host a session for patients and their families. Topics to be discussed during the session include:

- Starting treatment with Cystadrops® (cysteamine ophthalmic solution) 0.37%*
- Insurance coverage and paying for Cystadrops*
- Resources and support services available for patients*

10:20 am – 10:35 am Cystaran Update from Leadiant Biosciences, Inc. *Lesli King, Director of Marketing, North America*

10:35 am – 10:50 am **Horizon Therapeutics – Resources for the Cystinosis Community**
B.J. Viau (View) Director of Patient Advocacy, Rare Diseases

This talk will highlight and update you on a handful of the resources made available from Horizon Therapeutics. From educational books for kids and teens, to WBC testing kits. Walk away with one new resource for you &/or your family!

10:50 am – 11:20 am **AVROBIO - Investigational Lentiviral Gene Therapy for Cystinosis**
Fernanda Copeland, MS, RD, CDE, Global Head Patient Advocacy & Engagement, John Jeffrey Jones, Pharm. D, Associate Director, Clinical Scientist

**11:20 am – 11:50 am Disease Specific Quality of Life Questionnaires
IMPACT – Improvement of Motoric Abilities in Patients with Cystinosis
Newborn Screening Update**
*Katharina Hohenfellner, MD, Harald Schubert, Novotec
Cystinosis Research Network Funded Investigator*

The muscular state represents a crucial factor for the course of the disease. The involvement of the musculoskeletal system results in e.g. foot deformities, scoliosis and knock knees already occurring in childhood and adolescence in comparison to the healthy population. At the same time, there is an altered bone geometry with conspicuously thin corticalis. This compensatory change of the bone may be related to a low input of the muscle, similar to other chronic diseases. The positive influence of regular exercise in the form of various sports on the musculature was shown in our own patient collective with grip strength. Patients with an active lifestyle (n=16) showed normal grip strength, whereas the grip strength of patients without sports activities (n=53) was below normal. Based on these observations, the project presented here was developed, which, if successful, can be transferred to the general therapy concept for cystinosis patients as well as other patient groups with other chronic diseases. The concept presented here, follows the established approach for the rehabilitation of children "Auf die Beine", which was developed in Cologne for children and adolescents with limited mobility, e.g. caused by cerebral palsy or patients with osteogenesis imperfecta (<https://unireha.uk-koeln.de/kinder-jugendreha/behandlungskonzept-auf-die-beine/>). The training design with home exercise and short training sessions considers the fact that the target patient group is already under great strain due to the severity of the disease (medication, special diet, possibly dialysis). Patients train with Galileo vibration plates according to a fixed training schedule which provides for 10 short training sessions per week (maximum 2 per day). The control group will perform the same exercises without vibration plates, but with dumbbells. Patients will initially undergo an intensive training course and will receive regular supervision during the three-month home training phase. The study is designed as a randomized controlled trial. A baseline and two follow-up clinical assessment, one after the three-month home training phase and one after the follow-up phase, will take place. The primary endpoint is the change in muscle strength (in %) from the baseline examination to the measurement after the training phase. The Potential impact for patients with Cystinosis will be to positively influence the course of the disease themselves to improve muscle strength and quality of life.

11:50 am – 12:20 pm **Cognitive Control Systems in Cystinosis**
Ana Alves Francisco, PhD
Cystinosis Research Network Funded Investigator

Seminal behavioral studies in human patients have suggested the presence of cognitive difficulties in cystinosis. However, the neurocognitive phenotype associated with CTNS mutations and its developmental path are still poorly understood, and the prime areas of neurocognitive vulnerability in this population are in need of more thorough characterization. This is critical to developing effective therapies to compensate for or improve on areas of cognitive vulnerability. In this talk, we will focus on executive functioning, which refers to a set of cognitive processes that guide action and behaviors essential to aspects of learning and everyday human performance and contribute to the monitoring or regulation of performance. Executive function abilities—such as memory updating, set shifting, conflict monitoring, and inhibition—are critical for academic, professional, and social achievements and their impairment could explain some of the difficulties observed in cystinosis. We will present findings from a previous project funded by the CRN looking at inhibition and error-related processes in cystinosis and introduce our newly funded project, with which we aim to thoroughly characterize executive function in individuals with cystinosis in different age groups (and in their parents), utilizing a combination of behavioral, neural, and neuropsychological methods and focusing on four different components of executive function that may be accounting for the difficulties experienced by individuals with cystinosis: memory updating, set shifting, conflict monitoring, and inhibition. This multi-method approach, which will set the stage for further understanding of the cognitive and neural phenotype associated with cystinosis across development, is fundamental to understand mechanisms and associations between behavioral and neural activity and, ultimately, to define strengths and weaknesses in cystinosis and improve intervention and support.

12:20 pm – 1:00 pm **Break**

1:00 pm – 1:30 pm Validation Study of a New Biomarker for Cystinosis in a Retrospective Cohort from NIH

Elena Levtschenko, MD, PhD

Cystinosis Research Network Funded Investigator

Measuring white blood cell (WBC) cystine levels is a golden standard for the diagnosis of cystinosis and for monitoring cysteamine therapy. However, the laboratory technique for WBC cystine determination is laborious and is only available in a limited number of specialized laboratories. Moreover, because the pool of WBC cells is frequently renewed, WBC cystine levels reflect a short period of (adequate) cysteamine therapy. Our group has searched for alternative biomarkers of cystinosis and has found that the enzyme chitotriosidase (chito) might be a suitable candidate. Chito is released by activated macrophages which try to clear cystinosis tissues from cystine crystals. From the technical point of view, chito has several advantages such as the availability of easy and cheap method for its measurement, and the fact that the enzyme is extremely stable, allowing sending blood across borders on dry blood spots. We have found that plasma chito activity correlate with WBC cystine levels and kidney function of cystinosis patients in a cross-sectional (Elmonem et al. 2016) and a longitudinal (Vest et al. 2020) cohorts. Additionally, the occurrence of the extra-renal complications was associated with higher chito levels in adult patients (Vest et al. 2020). In the current project supported by CRN we aim to validate our findings in a large retrospective cohort of cystinosis patients followed at the NIH during a very long period of time. This long follow-up study aims to validate the clinical utility of chito as a novel long-term biomarker of cystinosis. Project title: Chitotriosidase as a therapeutic monitor for cysteamine therapy in cystinosis: a retrospective

1:30 pm – 2:00 pm Perturbations in the V-ATPase Pathway Drive Pathology in the Male Reproductive System in Cystinosis

Minnie Sarwal, MD, FRCP, DCH, PhD

Cystinosis Research Network and Cystinosis Ireland Funded Investigator

2:00 pm – 2:45 pm Parents of Children and Adults with Cystinosis Panel

Moderator: Jen Wyman, CRN VP Family Support

Panelists: Kristina Sevel, Jill Morrill, Chelsea and Brian Meschke

Panel presentation during which parents of children and adults with cystinosis will answer prepared questions and address topics related to the use of coping mechanisms through the ups and downs that cystinosis brings related to not only developmental and transitional issues of daily life but also medical issues. Parents of individuals at every stage of the disease will be featured and will share how they have managed the variety of challenges they have faced.

2:45 pm – 3:30 pm Adults Living with Cystinosis Panel

Moderator: Maya Doyle, MSW, PhD, LCSW-R

Panelists: Hannah Creel, Christina Morris, Brian Ensor, Gracie Smith

Panel presentation during which individuals living with cystinosis who serve on CRN's Adult Leadership Advisory Board (ALAB) will answer prepared questions and address topics related to the use of coping mechanisms and strategies for success through the ups and downs that cystinosis brings.