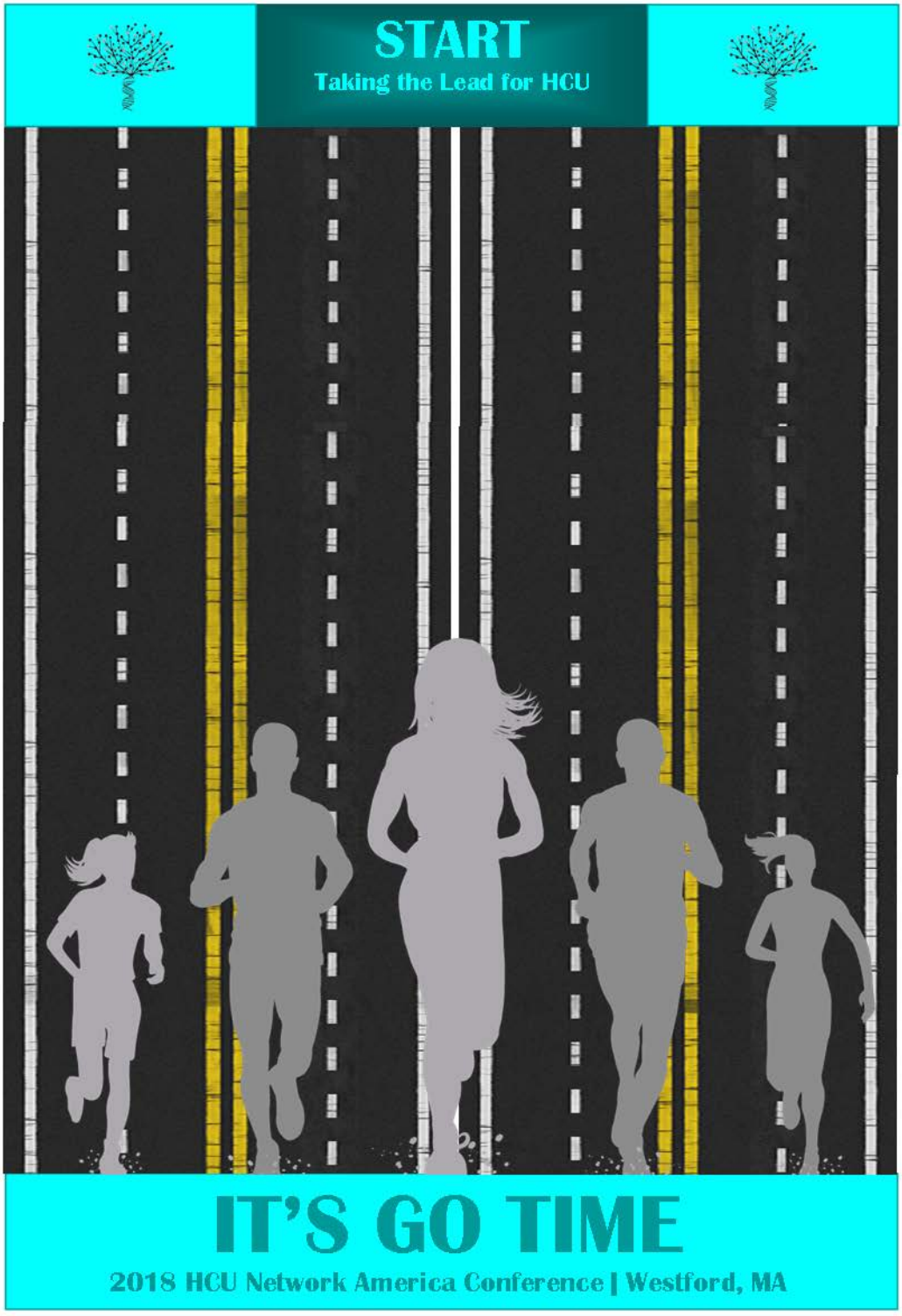
START
Taking the Lead for HCU
IT'S GO TIME
2018 HCU Network America Conference | Westford, MA

Contents – Outline of Report

A copy of the conference program, recording of the speaker conferences and panels, conference handouts, pictures from the conference, as well as interviews can be found on our conference website: https://hcunetworkamerica.org/2018-conference

Introduction

Individuals with homocystinuria and related disorders have a tremendous need for enhanced awareness, education, networking opportunities, and reassurance of management approaches available today and hope for even better therapies in the future.

Taking the Lead for HCU, HCU Network America's patient/family conference took place in Westford, Massachusetts on April 21-22, 2018. This inaugural conference was organized specifically for individuals with homocystinuria and associated disorders and their families. The main objective of the conference was disseminating sound information regarding best practices and research regarding Homocystinuria. This was achieved through patient and caregivers' sharing their experiences, healthcare professional's presentations, and HCU Network America and industry sharing information on research underway for new therapies in the future.

The second goal of our conference was to strengthen the dialogue between patients, caregivers and family members. Providing an opportunity for them to socialize, share and realize they are not alone in this journey is a very important part of the process.

Taking the Lead for HCU brought together 28 industry leaders and vendors, 10 medical professionals and over 70 patients, caregivers and relatives from all over the country.

This report presents an overview of the conference and provides a brief synopsis of the information each speaker or panel.

Participants

Speakers and Panelist
Dr. Kimberly Chapman: Metabolic Clinician, Children's National Hospital, Washington DC
Krista Viau: Dietitian, Boston Children's Hospital
Raenette Franco: Reimbursement Consultant, Compassion Works Medical, LLC
NextStep Organization: Cambridge, Massachusetts
Benjamin D. Goodlett: Psychologist, Boston Children's Hospital
Dr. Harvey Levy: Metabolic Clinician, Boston Children's Hospital
Margie McGlynn: President, HCU Network America
Patrick Horn: Chief Medical officer, Orphan Technologies
Panel: Moderator: Margie McGlynn, HCU Network America President
Expert: Dr. Harvey Levy, Boston Children's Hospital
Expert: Dr. Kimberly Chapman, Children's National Hospital, Washington DC
Patient: Kristin Rapp
Patient: Pamela Penrose
Parent: Sarah Sullivan

Key Organizers
Danae' Bartke – Conference Organizer, Executive Director HCU Network America
Lynn Paolella – Food and Beverage Organizer
Malathy Ramanujam – Food and Beverage Organizer

Sponsors

We thank our sponsors for making this meeting possible and for the compassion and support they show for the HCU Community.

Platinum Sponsors

orphan technologies

RECORDATI RARE DISEASES GROUP
Focused on the Few™

Silver Sponsors

CAMBROOKE THERAPEUTICS™

NUTRICIA Metabolics
Inspiring Futures

Bronze Sponsors

Taste Connections, LLC

Vitaflo®
Innovation in Nutrition

Non Profit Sponsors

NECPAD

A special thanks to the Hempling Foundation for Homocystinuria Research for funding the t-shirts.

Conference Outline

The conference took place over the course of two days, and was kicked off with an informal dinner meet-up the Friday evening before the conference. The purpose of the meet-up was to allow conference attendees the opportunity to meet, socialize get to know each other before the conference began.

The first day of the conference focused on general disease awareness and how to better manage Homocystinuria (HCU). The speakers and panelists we selected were able to provide information and expertise on Guidelines for Diagnosis and Treatment of CBS Deficiency, Dietary Practices, Medical Nutrition Reimbursement, Transitioning into Adulthood and HCU and the Brain. The information presented in day one was meant to create a clear understanding of what HCU is and how to effectively treat it.

Day two of the conference concentrated on the history and progress of homocystinuria, what lies ahead as well as how to drive it forward and create hope for the future. The speakers and panels we selected were able to provide information and expertise on the history of Homocystinuria and past and current Natural History Studies, Research and Strategy Map for Homocystinuria Therapies, Enzyme Replacement Therapy and a Patient – Expert Panel on Keys to Success. Also on day two, we awarded the first ever HCU Hero award to Dr. Harvey Levy for his lifetime of leadership and commitment to the HCU Community. We ended the conference with an open discussion with the community about what they thought our key priorities should be moving forward.

The sessions were recorded with the intent of archiving them to serve as educational resources for the overall homocystinuria community. In addition to the recorded sessions, we interviewed 4 patients from the HCU Community. By sharing their stories, we are reminded of the shared humanity and this helps strengthen and build understanding and awareness. You can find these recordings on our websites 2018 conference page as well as our YouTube Channel.

Summary of Presentations

Day 1: Awareness and Management

Guidelines for Diagnosis and Management CBS Deficiency – Kimberly Chapman
Dr. Kimberly Chapman was a member of the E-HOD Guidelines Committee and was responsible for gathering the data from a review of scientific literature that lead to the Guidelines for Diagnosis and Management of Cystathionine Beta-Synthase (CBS) Deficiency that were published in the 2017 Journal of Inherited Metabolic Disease.

Dr. Chapman briefly walked us through the biochemical pathways of the homocystinurias, what homocystinuria is and defined that her presentation would focus on a type of homocystinuria called Cysathionine Beta-Synthase (CBS) Deficiency, or classical Homocystinuria. She then went into detail about the affected systems, total homocysteine v. free homocysteine, and the total homocysteine goal for pyridoxine responsive and non-pyridoxine responsive patients. After defining the goal, she then explained the process of how your doctor will determine if you are pyridoxine responsive, and based on that assessment, what medications you would need and what the diet looks like. She then explained that prevention is key when it comes to avoiding cognitive delays, psychiatry disorders and thrombosis.

She also talked about the importance of taking the necessary preventative steps when planning a surgery and pregnancy. She closed by talking about what your clinic visit should look like.

Nutrition and Homocystinuria – Krista Viau
Krista Viau is a metabolic dietitian at Boston Children's Hospital. She has been working with children and adults with inherited metabolic disorders for 9 years. Krista is a recent addition to the Boston Children's team, having spent 8 years at the University of Utah Metabolic Clinic. Her research interests include studying the natural history of rare metabolic disorders and improving nutritional therapies for these conditions.

Krista started her presentation by describing the reasons for nutrition therapy in homocystinuria. She then provided resources and tools for tracking protein and methionine intake, and explained the rationale for tracking methionine vs protein. She closed by identifying management strategies, such as how best to plan, strategize, establish a routine, and distribute your protein and meal prep to ensure success with the low protein diet.

Medical Nutrition Reimbursement – Raenette Franco
Raenette is the founder of Compassion Works Medical and is a Certified Biller Coder Specialist (CBCS). This informative session was designed to help patients, parents and caregivers navigate reimbursement for medical foods, formula and supplements. During the presentation she walked us through insurance terminology, the difference between medical and pharmacy coverage, reimbursement issues between insurance company and supplier, billing discrepancies, verifying insurance benefits before placing an order and removal of medical food exclusion. You can see her subsequent webinar on our website at: https://hcunetworkamerica.org/insurance

HCU Network America has contracted Raenette to work with patients, families and caregivers one-one-one. As a result, her services are free to the HCU community. You can contact Raenette at: Raenettef@compassionworksmrs.com or (973) 832-4736

NextStep Organization - Panel
NextStep's program for people living with serious disease or rare genetic disorders helps these individuals develop life skills, find community and become self-advocates so they can move beyond their challenges to become strong, independent, productive adults. The program is co-designed by the young participants, health care professionals and NextStep to create a curriculum that addresses transitional issues and arms young people with tools, information and hope.

NextStep organization started off their presentation with information on the history of their organization, using a video to explain who they are. They then moved into an interactive discussion between their panel and attendees. During the panel, they touched on topics related to transitioning into adulthood, such as school, work, social life and medical care/benefits.

HCU and the Brain –Benjamin D. Goodlett
Benjamin Goodlett is currently a postdoctoral fellow in the Metabolism Clinic, Division of Genetics and Genomics, at Boston Children's Hospital. He provides neuropsychological assessments to children and

adolescents with metabolic disorders to monitor cognitive functioning, assist educational planning, and provide concrete recommendations for families. Ben also provides psychotherapy to children and adults impacted by metabolic disorders with a focus on family functioning, adherence to medically necessary behaviors, and finding an identity beyond diagnosis. His passion is helping families balance medical needs with everyday life.

Mr. Goodlett started his presentation with explaining the role of a psychologist in a metabolic clinic, noting that not all metabolic clinics have a psychologist. He then explained the potential impact on cognitive functioning in Homocystinuria patients. He notes that similar to most metabolic conditions, Homocystinuria patients tend to need tools and skills to help with executive functioning. He then presented examples and tools on how to increase cognitive functioning, and then talked about emotion changes with metabolic conditions including homocystinuria and the importance of metabolic control. For those with poor emotional control, he then presented a path of what to do to gain control over ones emotions. The last key point he touched on was social impact of homocystinuria, noting it doesn't just only affect the individual, but also relationships with the larger community. He also discussed triggers of stress, and offered coping strategies and communication techniques.

Day 2: History and the Future of Homocystinuria Treatment

Natural History Study – Dr. Harvey Levy

Dr. Levy developed a specific interest in Homocystinuria during his fellowship when he identified the first case diagnosed from newborn screening. Shortly thereafter he and Dr. Harvey Mudd discovered the first example of increased homocysteine due to a non-homocystinuric disorder, now known as cobalamin C defect. This was also the first example of a human disorder of vitamin B12 metabolism. Disorders of sulfur metabolism have continued to be a major interest of Dr. Levy's throughout his career. He has authored over 400 medical articles and book chapters on metabolic disorders, including many on the homocystinemias, and has received a number of national and international awards for his achievements.

Dr. Levy first talked about the impact patient and family organizations have had on patient communities. He talked about the isolation that patients and families felt when he first started practicing, and how that has changed with technology and the development of groups like HCU Network America. He noted the importance of being able to network, socialize and share the common experiences and information.

His first milestone in the history of homocystinuria described Dr. Nina A.J. Carson and her publication on the discovery of Homocystinuria. He explained that Dr. Carson's discovery came out of an interest for looking at patients for mental deficiencies. At that time, PKU was the only other metabolic condition noted for causing mental deficiencies.

He then explained the difference between methionine and homocysteine, with methionine being an essential amino acid that the body cannot produce on its own, that needs to be acquired from food. From there methionine gets metabolized to homocysteine, and then to cystathionine, but since homocystinuria patients cannot metabolize homocysteine into cystathionine, it instead recycles back to methionine.

He also talked about how many HCU patients are misdiagnosed with Marfan's Syndrome because of the similar symptoms, such as elongated limbs and dislocated lenses. Many years ago, Dr. Viktor McKusick

at Johns Hoplins was developing a program for medical genetics. He suggested to Dr. Schimke to do a urine test in the patients at the Marfan's clinic to see if maybe they were actually homocystinuria patients. From this came a study from Dr. Schimke's and Dr. McKusick's Marfan's clinic that identified 38 affected homocystinuria patients that had originally been misdiagnosed as having Marfan's syndrome.

Dr. Levy then talked about the effects of late diagnosed or untreated homocystinuria. He touched on the main problem areas that can result including intellectual disability, dislocated lenses, skeletal abnormalities and thromboembolism. From there he segued into the advances and problems with newborn screening for homocystinuria patients. He noted that Newborn Screening came about because of the Guthrie Test that was originally designed to diagnose Phenylketonuria patients. He talked about some of the different screening methods that have been used over time and noted that we now use tandem mass spectrometry. He noted that the issue with current newborn screening test is that patients don't always have elevated levels of methionine during the newborn screening period.

He then went on to explain that many of those who are missed by the current newborn test are pyridoxine (B6) responsive patients. He explained the difference between pyridoxine (B6) responsive and non-pyridoxine (B6) responsive patients, and how they test to see if a patient is B6 responsive or not. From there, he explained the goals of therapy, what therapy looks like and then what your target levels should look like. He notes that you should aim to get your levels as low as possible.

He briefly touched on the upcoming Enzyme Replacement Therapy Study and the current Natural History Study. He was involved in the last natural history study for HCU done in 1985. He noted though that you would expect results today to be very different, because many of the patients then were late diagnosed, not on diet, or not following their medical regimen. He gave details on the current Natural History Study for CBS deficient homocystinuria, including the applicant requirements, what it involves and the different areas assessed.

He ended with final thoughts, emphasizing that Homocystinuria is no longer the almost helpless disease it once was.

Research and Strategy Map – Margie McGlynn

Margaret (Margie) McGlynn is President of the Board of HCU Network America, a patient advocacy organization she co-founded to provide support for patients and families affected by homocystinuria. She is also President of the Hempling Foundation for Homocystinuria Research, a fund she established to support research on new therapies for HCU in honor of her late sisters, Judy and Susie Hempling.

Margie started her presentation with a video about her sisters, Judy and Susie, laying the ground work for why she co-founded HCU Network America and got involved in Homocystinuria.

She explained the goal of the Research and Strategy Map Project. The project helped identify current therapeutic approaches and those new approaches being researched, and highlighted the key priorities for future research that also guides prioritization for future research grants.

She explained that a consultant was hired who started with a search of the literature and clinical trail databases. She then solicited feedback on potential new approaches from and clinical and academic experts, as well as industry that have therapies in development for HCU. She then went into detail about the various novel approaches that are being investigated, that include Enzyme Replacement Therapy,

Gene Therapy, Alternative Enzymes, CBS Protein Activation, and Metabolic Pathway Modification and how they correlate to the biochemical pathway. From there, she went on to talk about each approach, where it is in its development pipeline, and the perceived strengths and benefits as well as weaknesses and limitations.

She then discussed the key priorities for future research and patient advocacy that were recommended by the experts interviewed, noting areas of optimizing current therapy, improving CBS Detection and advancing new treatment modalities, including better tasting medical foods and formula, as well as developing enzyme replacement therapies, alternative enzymes and potential gene therapies for HCU patients.

She then closed with information about the HCU Global Grants program, including the timeline for the current grant process. She ended with the additional next steps planned for the research grants process.

Enzyme Replacement Therapy – Patrick Horn
Patrick Horn recently joined Orphan Therapeutics where he is leading the clinical development of an enzyme replacement therapy for the treatment of Homocystinuria.

Dr. Horn started his presentation with the role of protein in the human body and how the decreased enzyme activity of Cystathionine Beta Synthase impacts Classical Homocystinuria patients. Then he went on to explain how current therapies do not correct all abnormalities associated with Homocystinuria. From there, he explained how Orphan Technologies drug, OT-58, would correct the abnormalities associated with Homocystinuria. He explained the proven beneficial effects in the mouse model.

After talking about OT-58, he talked about the drug development pathway and the steps it takes to getting a drug approved by the FDA. He noted there are 4 key crucial points to making new drugs available. It starts with basic research, then goes on to preclinical studies in animals to show safety and efficacy, safety and efficacy studies in humans and then finally approval. He also elaborated on what the entry criteria are for those who wish to enroll in the Enzyme Replacement Therapy human trials that are starting this fall.

He then closed with the importance the Natural History Study and the role it plays into developing new therapies. He noted that it's important to have enough patients enroll to really make the Natural History Study successful.

Patient Expert Panel: Keys to Success
A panel discussion was then held with patients and experts. These experts are active metabolic clinicians and researchers in the field of homocystinuria as well as other inborn errors of metabolism. The panelists also included two patients and one caregiver that have excelled at managing the disease while having all very unique backgrounds when it comes to diagnosis.

The moderator, Margie McGlynn, opened with introductions of each of the panel members. She started the discussion by asking the experts "what do you think is the most successful way to manage homocystinuria is". Both experts reiterated how important it was to follow the diet, take the formula, but to also be open and honest about any barriers that prevent you from doing so. This nicely segued into her next question which was addressed to Pam, a patient who wasn't diagnosed until she was in her mid-50s, "what was your secret to success"? She talked about how she didn't get a lot of information

from her dietitian about the diet, but rather about formula. She ventured out on her own and read everything she could and joined several communities to fully understand the diet. She had seen the other side prior to diagnoses through blood clots and strokes. She then asked the same question to Kristin, an adult patient who was diagnosed at birth. Kristin also runs marathons, which requires extra attention to diet. Kristin talked about the importance of formula, especially while she is preparing for a marathon. She also mentioned how social websites and low protein websites help her prepare nutritious meals she needs that follow the diet. The same question went to our last panelist, a parent of two young children who were missed by newborn screening, but were diagnosed after the older one had suffered a blood clot to the brain. She talked about how it's difficult with school, but it's important to have a schedule and support from the online community. She also talked about the support she gets from her clinic and the metabolic camp they offer that makes her children feel like part of a community that understands. Margie then opened the floor to the audience to ask questions. A final comment came for Dr. Levy when asked what he is most excited about for HCU patients – and he answered "hope for a better future". Which he believes will occur due to improved therapies like Enzyme Replacement Therapy that are in development.

Moving Forward: Input from the HCU Community

HCU Network America understands the importance of the role the HCU Community plays in the organization's past success and path forward, and values input from the community on what our priorities should be to best meet their needs.

We started the session with highlighting details of what we have accomplished so far, noting that everything goes back to the patients and better helping them on their journey. From there we opened up the floor to see what the community thought we needed to focus on, while also calling for volunteers who could help us complete our mission.

From the discussion that took place we realized our priorities and the communities needs were very in line. The community agreed that fundraising should be a priority so we can develop more resources, host future meetings and support research. Also, to assure the resources we develop best meet patient and family needs, and to support new families, we agreed that a patient/parent advisory board would be helpful. Based on the input, we have agreed to form two committees: a patient-parent advisory committee and a fundraising committee and many attendees volunteered to serve on one of these committees. Others are welcome to join. More information about these committees will be shared in a future edition of the HCU Herald, so please stay tuned.

HCU Hero Award: Dr. Harvey Levy


The first ever HCU Hero Award was presented by Dr. Harvey Levy, and is intended to be awarded at each patient/family meeting.

Following graduation from the Medical College of Georgia, Dr. Levy trained in pediatrics in Boston, New York, and Baltimore. Following pediatric training, Dr. Levy then completed a fellowship in metabolic disorders at the Massachusetts General Hospital (MGH) under Dr. Mary Efron, a pioneer in metabolism. After completing this training, Dr. Levy joined the faculty of the MGH and Harvard and also served as Consultant in Metabolism to the Massachusetts Newborn Screening Program. In 1978, Dr. Levy moved to Boston Children's Hospital to found and serve as Director of the Metabolic Program, now the Biochemical Genetics section of the Division of Genetics.

Dr. Levy developed a specific interest in homocystinuria during his fellowship when he identified the first case diagnosed from newborn screening. Shortly thereafter he and Dr. Harvey Mudd discovered the first example of increased homocysteine due to a non-homocystinuric disorder, now known as cobalamin C defect. This was also the first example of a human disorder of vitamin B12 metabolism. Disorders of sulfur metabolism have continued to be a major interest of Dr. Levy throughout his career. He has authored over 400 medical articles and book chapters on metabolic disorders, including many on the homocystinemias, and has received a number of national and international awards for his achievements. The HCU Community congratulates and thanks Dr.Levy for his dedication and contributions!