



THIRD INTERNATIONAL HOMOCYSTINURIAS PATIENT-EXPERT MEETING



28 FEBRUARY - 1 MARCH 2019, NH ROMA CENTRO, ROME

COLLABORATING PATIENT ORGANIZATIONS AND CONSORTIA



WELCOME

The organising committee welcomes you to Rome, the eternal city, for the Third International Homocystinurias Patient-Expert (IHoPE) Meeting. We are fortunate to bring together leaders in the field of homocystinuria research, clinical care, nutrition and advocacy for a two-day conference held in conjunction with Rare Disease Day 2019. The IHoPE Meeting promotes engagement and networking in the field of homocystinuria and provides a unique platform for the exchange of patient experiences and needs. This exchange of information is paramount when promoting improved health outcomes for individuals affected by these disorders.

We take this opportunity to thank each delegate and speaker for making the time to join us for IHoPE 2019 and we hope you are able to connect with, and learn from, others in the field of homocystinuria. We would also like to acknowledge and thank the sponsors for 2019; without them today would not be possible.



Carlo Dionisi-Vici
Italy



Henk Blom
Netherlands



Viktor Kozich
Czech Republic



Ida Schwartz
Brazil



Tara Morrison
Australia

OVERVIEW

Individuals with homocystinurias, methylation and folate defects have an enormous need for improved medical awareness, optimisation of the diagnostic process and treatment, and improved networking between healthcare professionals and patients.

THE AIMS:

- Provide stakeholders with updates on research and the possibilities for families and professionals internationally
- Strengthen networking between all stakeholders including enhanced peer-support by providing a face-to-face opportunity to meet
- Improve knowledge on these disorders by exchanging experiences and best practices on presentation, diagnosis, treatment and special circumstances
- Provide education and resources for patients and healthcare professionals
- Enhance stakeholder focus, knowledge and enthusiasm in these disorders
- Shared experience of individuals/caregivers living with these disorders

THE LEARNING OUTCOMES:

- Increase knowledge on frequency, pathophysiology, clinical manifestation and diagnosis of homocystinurias
- Understanding the complex and diverse aspects of treatment of homocystinurias
- Understanding the elements and interactions in the transsulfuration and remethylation pathways
- Understanding metabolism of related B-vitamins
- Insight into the principles and efficacy of newborn screening programs, and knowledge on efficacy of early intervention on short and long-term outcome
- Familiarizing with practical issues in diagnosing and treating patients with CBS deficiency and remethylation disorders
- Understanding new developments in treatment

PROGRAM: THURSDAY 28 FEBRUARY

8.00	Registration open	
08.30-10.30	SESSION 1: State of the art lectures	Chair: Ida SCHWARTZ
	Opening address:	Carlo DIONISI-VICI Tara MORRISON
	Metabolism	
8.30 - 8.50	Sulfur Amino Acids	Viktor KOZICH
8.50 - 9.10	Folate and B12	Henk BLOM
	Clinical Presentations	
9.10 - 9.30	CBS deficiency: Overview	Sufin YAP
9.30 - 9.40	CBS deficiency: A parents' perspective	Tara MORRISON
9.40 - 10.00	CblC and MTHFR: Overview	Carlo DIONISI-VICI
10.00 - 10.10	CblC: an adults' perspective	Francesca RESTUCCIA
10.10	COFFEE BREAK	
10.30-11.10	SESSION 2: Novel Developments in Remethylation Defects	Chair: Henk BLOM
10.30 -10.50	A transgenerational MMACHC epimutation illustrates a new mechanism of inborn errors of metabolism named epi-cblC	Jean-Louise GUEANT
10.50 -11.10	Structural basis of severe 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency	Matthias BAUMGARTNER
11.10 - 13.10	SESSION 3: Newborn screening	Chair: Alberto BURLINA
11.10 - 11.40	EHOD Recommendations on newborn screening for homocystinurias versus current practices	Martina HUEMER
11.40 - 12.00	Technical aspects of NBS in Homocystinurias	Giancarlo LA MARCA
12.00 - 12.20	Clinical management of a positive NBS for Homocystinurias	Alberto BURLINA
12.20 - 12.50	The outcomes in classical homocystinuria patients detected by newborn screening	Tawfeg BEN-OMRAN
12.50 - 13.10	Novel Developments in Remethylation Defects and Newborn screening: Q & A	Session speakers
13.10	LUNCH	
14.00 - 15.30	SESSION 4: Interactive Panel	Chair: Kimberly CHAPMAN
14.00 - 14.45	CBS deficiency	Viktor KOZICH Tawfeg BEN-OMRAN Sufin YAP
14.45 - 15.30	Remethylation disorders	Martina HUEMER Carlo DIONISI-VICI Matthias BAUMGARTNER Irina MANOLI
15.30	COFFEE BREAK	
	SESSION 5: New Developments	Chair: Viktor KOZICH
15.50 - 16.10	Microbiome in CBS deficiency	Ida SCHWARTZ
16.10 - 16.30	Arg to Cys mutation in CBS deficiency	Henk BLOM
16.30 - 16.45	Closing comments: Day 1	Henk BLOM Ida SCHWARTZ
17.00 - 18.00	NETWORKING CANAPES & DRINKS	

PROGRAM: FRIDAY 1 MARCH

8.00	Registration open	
08.30-10.30	SESSION 6: Long term outcomes	Chair: Carlo DIONISI-VICI
8.30 - 9.00	E-HOD Registry results: Remethylation disorders	Martina HUEMER
	E-HOD Registry results: CBS deficiency	Viktor KOZICH
9.00 - 9.20	The Irish Experience	Gregory PASTORES
9.20 - 9.40	Observational study of the natural history of patients with classical homocystinuria on current therapy	Marcia SELLOS-MOURA
9.40 - 11.00	SESSION 7: Recent advances in novel treatments	Chair: TBC
9.40 - 10.00	Enzyme replacement therapy for classical homocystinuria	Tomas MAJTAN
10.00 - 10.20	Impact of EPI743 on visual function in cblC defect	Diego MARTINELLI
10.20 - 10.40	Progress in CblC treatment	Irina MANOLI
10.40 - 10.50	Treatment of cobalamin metabolic disorders with oh-cobalamin through an "in situ" subcutaneous permanent catheter: reaching the goal.	Andrea BORDUGO
10.50 - 11.00	Long term outcomes and novel treatments: Q & A	Session Speakers
11.00	COFFEE BREAK	
11.20 - 13.00	SESSION 8: Living with homocystinuria	Chair: Ida SCHWARTZ
11.20 - 12.00	Dietary practices in pyridoxine non-responsive homocystinuria and the impact of E-HOD guidelines	Marjorie DIXON Alexandra JUNG
12.00 - 12.15	RMD calculator& platform- tools supporting HCU diet calculation and communication between HCP & patients	Iwona BARTLOMIEJCZYK
12.15 - 12.25	Classical Homocystinuria in Qatar: Nutritional advances and challenges	Reem AL-SAAD
12.25 - 12.40	The challenges of parenting a child with phenylketonuria (PKU): Parents' lived experiences	Anja WITTKOWSKI
12.40 - 12.45	Growing up with classical homocystinuria: a child's perspective.	Owen AUSTIN
12.45 - 13.00	Living with homocystinuria: Q & A	Session speakers
13.00	LUNCH	
14.00 - 15.30	SESSION 9: Patient Organisations	Chair: Tara MORRISON
14.00 - 14.20	Global Research Map and Grants Process for HCU	Margie MCGLYNN
14.20 - 14.40	Homocystinuria Patient and Caregiver Survey: Experiences of Diagnosis and Patient Satisfaction	Tara MORRISON
14.40 - 15.00	Cblc onlus, from the beginning until now	Rossella BRINDISI
15.00 - 15.20	cblC Brazil - News and Progress	Luana BRITO
15.20 - 15.30	Closing comments: Day 2	Henk BLOM Ida SCHWARTZ
	Acknowledgements	Carlo DIONISI-VICI Tara MORRISON
15.30	CLOSE	

SPEAKERS



VIKTOR KOZICH

Professor Kožich graduated from the School of General Medicine, Charles University in Prague in 1985. Since his graduation he has been working in the Institute of Inherited Metabolic Diseases and he specialized in clinical biochemistry and medical genetics, in 2012 he became the full Professor of Medical Genetics.

His main interests are genetic, biochemical, clinical, epidemiological and ethical aspects of inherited metabolic disorders with a special interest in disorders of homocysteine metabolism and namely in cystathionine beta-synthase deficiency—a disease in which he became interested in 1991-1992 during his fellowship in the laboratory of Prof. Jan P. Kraus (University of Colorado School of Medicine in Denver, USA). Prof. Kožich is also involved in organization of neonatal screening and serves as a Chairman of the national Coordination Center on Neonatal Screening in the Czech Republic.

Professor Kožich has been a tutor of graduate and postgraduate students, he is an author of over 100 publications in peer reviewed international journals, several chapters in books, and of articles and chapters in Czech medical literature; he has been an invited speaker at various international and national conferences. He is a member of councils of several international learned societies (SSIEM, ERNDIM, and ESHG) and he is active in peer review system at both the national and international levels.



HENK BLOM

Henk Blom finished his Chemistry study in 1985 and received his PhD in 1988 at the Radboud University Nijmegen. After his post-doc period at the Human Genetics Branch, NIH, USA (William Gahl), he became post-doc in 1990 and later in 1992 staff member of the Clinical Genetics Center Nijmegen at Laboratory of Pediatrics and Neurology, University Hospital Nijmegen, the Netherlands. In 1997 he became Established Investigator of the Netherlands Heart Foundation and in 2003 he was registered as Clinical Biochemical Geneticist. In 2007 he was appointed as vice-head and later head of the Metabolic Unit at the Department Clinical Chemistry, VU University Medical Centre Amsterdam, the Netherlands and in 2009 he became Professor in Biochemistry of Inherited Metabolic Diseases at the VU University Medical Centre Amsterdam. Since 2014 he is head of the laboratory for Clinical Biochemistry and Metabolism, Department of General Pediatrics, Center for Pediatrics and Adolescent Medicine University Hospital Freiburg, Germany.

His research concerns inborn errors of metabolism with special focus on inherited defects of homocysteine, methylation and folate metabolism. His contributions include the association of a disturbed homocysteine metabolism with pregnancy complications, including neural tube defects, cardiovascular disease, thrombosis and stroke in children. He investigated the genetic etiology of thermolabile MTHFR, which resulted in the discovery of the MTHFR 677C>T variant which is the first identified genetic risk factor for neural tube defects. Basic research concerned the effects of homocysteine and its metabolites on development of chicken embryos and endothelial function.

Among inborn errors of metabolism his group described the molecular basis of severe hyperhomocysteinemia. They also explored cystinosis and defects in the methionine methylation pathway, including methionine adenosyltransferase deficiency. They discovered

two new genetic defects: one in folate metabolism: dihydrofolate reductase deficiency and one defect in methylation: adenosine kinase deficiency. Prof Henk Blom is coordinator of E-HOD, an international consortium on homocystinurias and methylation disorders. In 2017 the consortium consisted of almost 100 partners. Main achievements are the setup of the E-HOD registry (www.EHOD-registry.org) and website (www.E-HOD.org) with information for expert as well as patients and their families. In addition four guideline manuscripts have been published, teaching courses and Patient - Expert Meetings organized.

He supervised as (co)promoter of 31 PhD students and published over 350 papers in international journals resulting in an H-index of 72.



SUFIN YAP

Professor Sufin Yap is a Consultant Paediatrician in Metabolic Medicine at Sheffield Children's Hospital and an honorary senior lecturer at the University of Sheffield, UK, since 2012. She was formerly a Consultant Metabolic Paediatrician at the National Center for Inherited Metabolic Disorders, Dublin and Professor of Paediatric Metabolic Medicine at University Malaya. She graduated from the Royal College of Surgeons in Ireland and received her Doctorate on Classical Homocystinuria in 2000.

Six of her published works on homocystinuria were selected in three consecutive years at the Irish Journal of Medical Science (IJMS) Doctor / Royal Academy of Medicine Ireland (RAMI) Awards for excellence in clinical research (2000-2002). She was the recipient of the IJMS/ RAMI Award for the "Risk Factor Medicine" category in 2001 for her vascular work on homocystinuria and of the Royal Academy of Medicine Ireland Paediatric Registrar Medal in 2001 for work published on the effects of early dietary treatment in the prevention of mental retardation in patients with homocystinuria.

Her clinical interests are in nutritional treatment and inherited metabolic disorders, particularly homocystinuria and its obligate carriers. She has a long and vast clinical and research experience in managing Inherited Metabolic Disorders. Her current research interests include work on the vascular component in homocystinuria and inherited thrombophilia aimed at evaluating current treatment regimens in reducing vascular risk and is the chief investigator for the European PROTECT study on the long term treatment of organic acidurias. She has more than 100 international presentations, publications and abstracts. Her other interests include disseminating knowledge on management of metabolic diseases in the Far East, assisting in developing skills and techniques for investigative tests to be available locally, and treatment in acute metabolic encephalopathies.



TARA MORRISON

Tara Morrison is director and chair of HCU Network Australia. Her connection to this disorder is a personal one: her two sons were diagnosed with Classical Homocystinuria at ages 5 and 1 years. At the time of diagnosis the Morrison Family were left with many unanswered questions. Their response has been to try and change this experience for others.

In 2014 Tara founded HCU Network Australia and serves voluntarily as Director and Chair of the Board. She is eager to utilize her personal and professional experience to achieve real outcomes for individuals affected by the disorder and their families.

Tara has practiced law in private practice for the past 10 years. She has worked in a range of areas and specializes in family law and building and construction. Tara holds a double degree in Arts and Law. She is a solicitor admitted in NSW and the High Court of Australia.



CARLO DIONISI-VICI

Dr. Carlo Dionisi-Vici, pediatrician is Head of the Unit of Metabolic Diseases at the Bambino Gesù Children's Research Hospital in Rome, Italy. His clinical and research focus includes translation research in inborn errors of metabolism (organic acidaemias, urea cycle defects, homocystinurias, fatty acid oxidation and carbohydrate related disorders, mitochondrial, lysosomal, and autophagy disorders). Main focus include acute and long-term management, new technologies to improve diagnostic processes by biomarkers analyses, and development of guidelines. He actively participates in the MetabERN network and current project is U-IMD (Unified Registry for Inherited Metabolic Disorders)



FRANCESCA RESTUCCIA

I was diagnosed with Homocystinuria with cobalamin CblC deficiency when I was 22, after 10 months of recoveries and exams without a clear medical diagnosis. My life totally changed, in fact now I use a wheelchair but I can say I'm a very lucky girl. I started again to follow my goals but with a new perspective and more awareness. I wanted to become a healthcare professional and I graduated in social work studies; now I work with people with Alzheimer and Dementia in a rehabilitation project and I have also other projects to achieve. My hope for the future is a more effective therapy for Homocystinuria, especially for those children that have more severe symptoms and consequences than me.



JEAN-LOUISE GUEANT

Professor Jean-Louis Guéant is Head of Department of Biochemistry-Molecular Biology and Nutrition of University Hospital of Nancy, Director of UMR-S Inserm 1256 "Nutrition-Genetics-Environmental Exposure" at the University of Lorraine, and coordinates the Federation of Clinical Research ARRIMAGE.

In France, he is President of the 44th section (Medical Biochemistry-Molecular Biology, Physiology, Cell Biology and Nutrition) of the National Committee of Universities (evaluation recruitments and careers), President of the National Commission of Medical Biology, and Member of the National Academy of Medicine.

He has organized four international congresses since 2010 and is regularly invited to international conferences as speaker and session chair. He is member of the editorial board of Hum Genet and reviewer for high impact journals such as N Engl J Med, Cell Metab, Circulation, Gastroenterology, Gut, and Am J Clin Nutr.

His scientific production includes 377 articles in Pub Med. He has described key mechanisms of digestive transport and metabolism of vitamin B12 and folate, the role of epigenome, cellular stress, energy metabolism and fetal programming in rare and complex metabolic diseases and a new type of B12 rare disease named "Epi-cblC." and has dissected the genetics of allergic drug reactions, with publications in N Engl J Med, Nat Comm, Lancet, PNAS, Ann Intern Med, Gastroenterology, Gut, J Hepatology, Nucleic acid Research, J Allergy Clin Immunol, and Blood.

He has received the Distinguish Scientist Award of the Sigrid Juselius Foundation, the AGAF award of American Gastroenterological Association, and the "Prix Elise Cailleret" of the French National Academy of Medicine.



MATTHIAS BAUMGARTNER

Prof. Dr. med. Matthias R. Baumgartner studied Medicine at the University of Basel, Switzerland, where he earned his degree as a medical doctor in 1992. He then went on to do a postgraduate course in experimental medicine and biology at the University of Zurich followed by laboratory work at the Biocentre of the University of Basel. After completing his residency in pediatrics at the University Children's Hospital Basel and at Hôpital Necker - Enfants Malades in Paris, Prof. Baumgartner continued his training in the United States, where he worked as postdoctoral and clinical fellow at the Mc Kusick-Nathans Institute of Genetic Medicine at Johns Hopkins University, Baltimore, from 1999-2001. He returned to Basel to lead the Metabolic Unit at the University Children's Hospital. 2 years later Prof. Baumgartner joined the Division of Metabolism & Molecular Pediatrics at the University Children's Hospital in Zurich. After his habilitation in 2005 he was elected as professor for metabolic diseases at the University of Zurich in 2008. Prof. Baumgartner is head of the Division for Metabolic Diseases, Medical Director of the Swiss Newborn Screening Program and since 2017 Director of the Children's Research Center at the Kinderspital Zürich. Since 2012 he leads the clinical research priority program "Rare Disease Initiative Zurich - radiz" at the University of Zurich. He is an internationally known metabolic paediatrician and scientist with a main research interest in disorders of intracellular cobalamin metabolism including the homocystinurias and methylmalonic acidurias; he is a steering committee member of the European networks and registries for Homocystinurias and remethylation disorders (E-HOD, www.e-hod.org) and Intoxication type Metabolic Diseases (E-IMD, www.e-imd.org) and an editor of the Journal of Inherited Metabolic Disease.



MARTINA HUEMER

Professor Huemer is a Pediatrician (Senior consultant) and psychologist. Specialist for inborn errors of metabolism with continuous engagement in clinical and research activities in the field since 1996.

Medical career: Pediatric University Hospital Vienna (Prof. S. Stöckler) 1995-2001, LKH Feldkirch (2001-2006), LKH Bregenz since 2007, additionally member of staff at the Pediatric University Hospitals in Zurich and Basel since 2009. Habilitation treatise on "Homocysteine, cobalamin and folate metabolism in children and adolescents" (University of Vienna 2009).

Several projects and peer reviewed publications on homocysteine metabolism and methylation disorders.

Clinical work (care for in- and outpatients with inborn errors of metabolism) at the Pediatric University of Basel, and at the LKH Bregenz.

Member of the Austrian and Swiss Groups of inborn errors of metabolism, EHOD, and of the SSIEM. Active participation in the international guideline groups for urea cycle disorders, Pompe's disease, Gaucher's disease, remethylation disorders and methylmalonic aciduria/propionic aciduria.



GIANCARLO LA MARCA

Assistant Professor of Pharmacology, granted by the University of Florence, since November 1st 2007

- Deputy Head of Newborn Screening, Clinical Chemistry and Pharmacology Lab, Meyer Children's Hospital, Florence, Italy, since 2011
- Associate Professor of Clinical Biochemistry and Clinical Molecular Biology, granted by the University of Florence, since November 1st 2015
- Qualified as full Professor of Clinical Biochemistry and Clinical Molecular Biology, granted by the University of Florence, since November 1st 2016
- He is 2018-20 President of the Italian Society for Newborn Screening and Metabolic diseases (SIMMESN)
- He is a member of the CLSI (Clinical Laboratory Standard Institute) Advisory Board for the revision of USA Guidelines on Expanded Newborn Screening by Tandem Mass Spectrometry
- He is a member of the Italian Council for Expanded Newborn Screening by Tandem Mass Spectrometry, Ministry of Health
- He is coordinator of some national research granted projects

Prof. La Marca has been an invited lecturer to more than 120 national and international meetings and he has authored more than 150 peer-reviewed publications and 5 patents dealing with areas of, clinical chemistry, mass spectrometry pharmacology and paediatrics. He serves as a reviewer for many scientific journals including The New England Journal of Medicine and Blood

Total IF >500; H Index 36

Prof La Marca received several awards in his career:

- Porcellino Prize 2011 by City of Florence for research activity in pediatric preventive medicine

- Young Researchers Prize 2012 Meyer Hospital/University of Florence for research in pediatric clinical chemistry
- Paul Harris Prize 2012, for research in pediatric preventive medicine
- "Excellence of the Year" prize, 2013, Lions Club, Scandicci, Florence
- American Academy of Immunology: award for "one of the best research on immunodeficiencies of the year 2013"
- International Society for Neonatal Screening: ISNS Dussault Medal 2014 to "honour a researcher who has made a significant contribution to neonatal or other population-based screening which is recognized as such".
- Voa Voa Award 2015: "For personal and professional commitment made in the pediatric research and application of concrete scientific solutions for the benefit of society as a whole".



TAWFEG BEN-OMRAN

Dr. BEN-OMRAN received his speciality training in clinical & metabolic genetics at the Hospital for Sick Children, University of Toronto, Canada. He has obtained both FRCPS & FCCMG in Medical Genetics in 2006. Currently, he is the Chief of Clinical and Metabolic Genetics Division in Qatar. He is an Associate Professor at Weill Cornell Medical College, Qatar & New York-USA. He is also a Distinguished Visiting Scientist at Boston Children's Hospital-USA.

He contributes to the body of published knowledge in clinical and metabolic genetics, with over 90 published articles in peer reviewed journals, book chapters and abstracts. He is reviewer for many clinical genetics journals.

He is an active clinical researcher, collaborating on projects with local, regional & international communities. He is a lead primary investigator in many high profile research projects & clinical trials to evaluate the long-term effects of enzyme replacement therapy in patients

with different lysosomal storage disorders. His main scientific interests include genetics of brain malformation & microcephaly, white matter disorders, dysmorphology, autosomal recessive disorders. In addition, Dr. Ben-Omran is an external advisor and expert for E-HOD (European registry and network for homocystinurias and methylation defects).

He is recognized as an expert in genetic disorders of the Arab population. His national & international presence is clear. In 2013, he received the "Princess Aljawhara Center Award for The Best Research in Basic Genetics" the most competitive & prestigious awards. He received Research Award from MRC-HMC for Homocystinuria project and Stars of Excellence Award 2011 for both Pioneering Newborn Screening & specialized care of Genetic Diseases in the Middle East. Recently, awarded the Stars of Excellence in research 2014: Cutting Edge of Research in Medical Genetics.

He has memberships in many societies including: American Society of Human Genetics, European Society of Human Genetics, Society for the Study of Inborn Errors of Metabolism, Middle East Metabolic Genetic Group, the Middle East & North Africa Newborn Screening Initiative, Middle Eastern Lysosomal Storage Diseases Expert Council Advisory Board, Child Health Research Advisory Committee, International Society for Prenatal Diagnosis, Chairman of Middle East Metabolic Dieticians Group & Founder Member & Regional Representative of SSIEM Adult Metabolic Physicians Group.



KIMBERLY CHAPMAN

Dr. Kimberly Chapman is a physician and scientist at the Children's National Rare Disease Institute in Washington, DC, USA. She graduated with an MD and a PhD from the University of Nebraska and then completed her internal medicine and pediatric residencies at the University of Pittsburgh Health Sciences Center. She went on to do medical

genetics training at the Children's Hospital of Philadelphia and joined the staff at Children's National Health System (CNHS) in 2010. Her clinic interests focus on the propionate pathway disorders and homocystinurias. Dr. Chapman's laboratory studies the interaction of several metabolic pathways and their impact on the Krebs cycle.



IDA SCHWARTZ

Ida Vanessa D. Schwartz graduated in 1994, entered residency in clinical genetics in 1995, started her Master's degree program in 1998, her PhD in 2000 (this last post graduate course ended in 2004), and started her Postdocs in 2015 and in 2016 respectively. Both her Master's and her PhD were related to inborn errors of metabolism, and the study of ethical/economic aspects related to the treatment of rare disorders is one of her main research lines. She is an associate professor of the genetics department at Universidade Federal do Rio Grande do Sul (UFRGS), as well as the coordinator of both the local Gaucher Reference Center and the Inborn Metabolic Clinics in the Medical Genetics Service at Hospital de Clínicas de Porto Alegre, Brazil, which is an international reference center for the diagnosis and treatment of lysosomal storage disorders. Among the awards and recognitions she has received, some stand out, such as, the L'OREAL/Brazilian Academy of Sciences for Women in Science (2007) and her affiliation to the Brazilian Academy of Sciences (2008). She has been a member of the Ethics Committee of UFRGS since 2011.



GREGORY PASTORES

Gregory M. Pastores MD is Clinical Professor of Medicine (Genetics), University College Dublin, Ireland, and Consultant with the Adult Metabolic Service/Department of Medicine/National Centre for Inherited Metabolic Disorders at the Mater Misericordiae University Hospital, Eccles Street, Dublin 7, Ireland. He is also currently National Speciality Director (Genetics) for the Republic of Ireland.

A graduate of the University of Sto. Tomas in Manila (1983), he trained in Pediatrics and Genetics at the Mount Sinai Medical Center in New York (1989) and at the Mayo Clinic in Minnesota (1991). While at Mount Sinai, he received the Young Pediatric Investigator Award, Mount Sinai Child Health Research Center, NIH (5 P30 HD28822), 1993-1996, and the Clinical Associate Physician Award, Mount Sinai General Clinical Research Center, National Center for Research Resources, NIH (5M01-RR0071), 1996-1997. Prior to coming to Ireland, he was an Associate Professor of Neurology and Pediatrics at the NYU School of Medicine in New York, and Director of the Neurogenetics Laboratory for the Department of Neurology at NYU in New York (1997-2013).

Dr. Pastores has extensive clinical and research experience in the diagnosis and management of patients with the lysosomal storage disorders, and was engaged in the development and testing of treatments for Gaucher, Fabry, MPS I, IV and VI, Pompe disease and a late (adult)-onset form of Tay-Sachs disease (GM2-gangliosidosis). He has published over 250 papers, 25 book chapters and three textbooks, including the recently released *Lysosomal storage diseases: Pathobiology and Therapeutic Considerations* (2016).



MARCIA SELLOS-MOURA

Marcia Sellos-Moura, PhD, is Vice President of Program and Portfolio Management at Orphan Technologies, a company dedicated to developing novel therapies to dramatically improve the lives of patients suffering from the rare disorder homocystinuria and related diseases. Prior to joining Orphan Technologies in 2016, Dr. Sellos-Moura held a variety of positions of increasing responsibility at Shire and Transkaryotic Therapies and was an integral contributor to the approval of four products and to the development of greater than 20 candidates across their rare disease portfolios. She has over 20 years of research, development, and program management experience with emphasis in preclinical and clinical development as well as bioanalytical and translational sciences. Dr. Sellos-Moura holds a PhD in Biochemistry, Cell and Molecular Biology and a bachelor in Biochemistry and Chemistry from Cornell University, as well as a graduate degree in Biopharmaceutical International Regulatory Affairs.



TOMAS MAJTAN

Tomas Majtan received his PharmD in 2003 from the Faculty of Pharmacy, Comenius University in Bratislava studying novel antimicrobial compounds and disinfectants using Salmonella pathogens. He then pursued postgraduate training in microbiology at Slovak Medical University and in 2006 he received a PhD in molecular biology working at the Institute of Molecular Biology of the Slovak

Academy of Sciences. During this period, he studied epidemiology and genetics of Salmonella virulence factors and antibiotic resistance markers and deciphered gene expression of bacteriophage during infection of an important industrial strain producing amino acid lysine. In 2007, he started postdoctoral training on enzymology and biochemistry of cystathionine beta-synthase (CBS) in Professor Jan Kraus group at the University of Colorado School of Medicine, Aurora, Colorado. In 2013, he was promoted to Assistant Research Professor at the Department of Pediatrics, Section of Genetics and Metabolism, University of Colorado School of Medicine and continues working on understanding molecular mechanisms behind inborn errors of metabolism and developing new treatments with focus on homocystinuria.

His contributions to the field include uncovering the mechanism of how missense pathogenic mutations impair CBS function, understanding how CBS cofactors work and affect folding and stability of the WT and mutant enzyme, solving several crystal structures of full-length human CBS to gain structural insight into homocystinuria or clarifying the role of CBS as hydrogen sulfide producing enzyme in health and disease. He utilized his intimate knowledge about CBS and has been working with Professor Jan Kraus and Orphan Technologies on enzyme replacement therapy for homocystinuria since 2010.

Dr. Majtan has been a mentor and supervisor of several graduate and postgraduate students or research associates. He is an author of over 40 peer-reviewed papers published in international journals as well as several patents, book chapters and monographs. He regularly presents his research on various conferences and meetings. In addition, he serves as a reviewer for multiple scientific journals and several funding agencies.



DIEGO MARTINELLI

Dr Diego Martinelli got his Medical Degree in 2003 at the Sacred Heart Catholic University, Rome, Italy, with a thesis entitled "Role of thalamo-cortical circuits in the determinism of CSWS in sleep: clinical study in childhood" (Supervisors Prof. Franco Guzzetta -Institute of Child Neuropsychiatry, "A. Gemelli" Hospital, Rome - and Prof. Concezio Di Rocco -Institute of Neurosurgery, "A. Gemelli" Hospital, Rome). He got in 2009 the Board certification in Child Neurology and Psychiatry, Sacred Heart Catholic University, Rome, Italy and in 2012 his PhD in Neuroscience of development at the Institute of Pediatrics of the Hospital "A. Gemelli", Sacred Heart Catholic University, Rome, Italy. His clinical and research focus was based on the study of Neuromuscular disorders (diagnosis, therapy, follow up and rehabilitation). From 2009 to 2014, he was clinical and research fellow at the Division of Metabolism and Laboratory of Metabolic Biochemistry of ad Bambino Gesù Children's Hospital, IRCCS of Rome (Head Dr. Carlo Dionisi-Vici). His clinical and research program was based on the study of inherited metabolic diseases (IEMs) in children, with a particular focus on mitochondrial diseases, copper metabolism disorders, neurodegenerative diseases, neurocutaneous diseases, urea cycle defects and organic acidurias. From 2014-2016 he was Post-Doctoral Visiting fellow at the Section of Translational Neuroscience, Molecular Medicine Program, Eunice Kennedy Shriver National Institute of Child Health and Human Development/National Institute of Health (NICHD/NIH) (Supervisor Dr. Stephen G. Kaler). During those years, his research activity was aimed at elucidating the pathomechanisms of copper metabolism disorders (MENKES and MEDNIK diseases) by using cellular and animal models. He also participated to an AAV-mediated brain-directed gene therapy approach in a mouse model of MENKES disease. In 2016, he was appointed as confirmed Physician at the Division of Metabolism, Bambino Gesù Children's Hospital, IRCCS in Rome. In 2018,

he got the National Qualification as Associate Professor of Medial Genetics. His main scientific and clinical activity is devoted to the study of IEMs, including:

- Homocystinurias and Remethylation disorders
- Mitochondrial Disorders
- Metal disorders
- Organic acidemias
- Urea Cycle Defects & related disorders (HHH Syndrome - LPI)
- Neurometabolic disorders
- Neuromuscular disorders
- Metabolome analyses
- Gene therapy
- Animal models
- Genome Editing
- Intracellular trafficking and Signal Transduction

Dr Martinelli participates in multiple translational research projects, mainly focused on identifying new disease gene and biomarkers, novel therapeutic approaches and on the development of functional scale and guidelines for IEMs. He is author of more than 80 articles and reviews in peer-reviewed international journals, as well as numerous chapter in books on IEMs. He is a member of SSIEM (European Society for the Study of Inborn Errors of Metabolism), Vice-president of SIMMESN (Societa' Italiana per lo studio delle Malattie Metaboliche Ereditarie e lo Screening Neonatale). He is PI and Co-PI of numerous clinical trials for IEMs, including the first trial of an antioxidant drug to treat visual defect in Cobalamin C defect. He participates to several International consortia for IEMs (E-IMD, E-HOD) and is a regular member of the working groups for European Guidelines for Urea Cycle Disorders, Homocystinurias and remethylation disorders, and Methylmalonic/Propionic Acidurias.



IRINI MANOLI

Irini Manoli, M.D., Ph.D., is a physician scientist and clinician associate investigator in the Organic Acid Research Section of the National Human Genome Research Institute (NHGRI), National Institutes of Health (NIH), in Bethesda, MD, USA. She received her M.D. from the University of Athens, Greece and subsequently pursued residency training in pediatrics and neonatology in the UK. She pursued postgraduate training including a M.Sc. in pediatric endocrinology and a Ph.D. in basic medical sciences, at the University of Athens, Greece. She then worked on mitochondrial genomics as a postdoctoral fellow at the National Center for Complementary and Alternative Medicine, NIH and subsequently trained in genetics and clinical biochemical genetics, at the Medical Genetics Branch, NHGRI, NIH, Bethesda, MD and was board certified in 2009.

Her primary interest is in combining work on animal models and clinical studies with the aim to develop new therapies for methylmalonic acidemias (MMA) and defects of intracellular cobalamin metabolism. Her work was critical in the reappraisal of dietary practices for MMA and cobalamin C deficiency in the USA and the development of improved guidelines for these disorders. She has worked with several mouse models of defects in the cobalamin pathway, studying the pathophysiology underlying disease manifestations, discovering new disease biomarkers and testing small molecule therapies. Along with the work in the lab, she takes care of the patients enrolled in the NIH clinical protocol on MMA and cobalamin disorders and works on translating preclinical therapies from animal models of MMA into the clinic.



ANDREA BORDUGO

Since the beginning of 2014 Dr Andrea Bordugo has been the Head of Inherited Metabolic Disease Unit and Clinical Chief of the Expanded Newborn Screening Program at University of Verona, Italy.

From 2009 to 2014 he was metabolic disease pediatrician at Metabolic Disease Unit of Padua University, Italy, with Professor Alberto Burlina

From 1997 to 2009 he was appointed as leading doctor for genetic and renal pediatric disease at Pediatric and Neonatology Department, Pordenone, Italy.

He have been involved in training experinces at Kings' College Hospital and Great Ormond Street Hospital, London, in the field of rare neonatal and children diseases.

He is member of the Council of the Italian Inherited Metabolic Disease Society(SIMMESN).

He published works and papers on inherited metabolic diseases.



MARJORIE DIXON

Marjorie Dixon qualified as a dietitian in 1981 with a BSc in Nutrition and Dietetics from Robert Gordon's Institute of Technology, Aberdeen, Scotland. Marjorie joined the Dietetic Department at Great Ormond Street Hospital for Children, London in 1983 as a paediatric dietitian. Marjorie is the Clinical Lead Dietitian for Metabolic Medicine and has specialised in the dietetic management of children with inherited metabolic disorders for over 30

years. She is primarily a clinical dietitian but is also involved in teaching (at national and international level) and research work. She has been a council member of The Society of Inborn Errors of Metabolism (SSIEM), is now a committee member of SSIEM-Dietitians Group and is an active member of the BIMDG-Dietitians Group, UK. Marjorie is an Honorary Lecturer at the University of Plymouth. She is lead dietitian for the Dietetic management of Inherited Metabolic Disorders module for the MSc in Advanced Professional Practice in Paediatric Dietetics, University of Plymouth. She is co-author of the Dietary Management of Inherited Metabolic Disorders section in Clinical Paediatric Dietetics, Wiley, 4th edition, 2015.



ALEXANDRA JUNG

Alexandra Jung, Diplom-Oecotrophologin

Alexandra Jung has a degree in nutrition science (Diploma) and a master in humanitarian assistance.

She is working as a dietitian in the Competence Center for Rare Metabolic Disease, Charité, Berlin since 2013.

Her focus lies on being a consultant for adults with metabolic diseases. In addition, she is working as a pediatric dietitian in the children hospital, being involved in the process of transition.



IWONA BARTŁOMIEJCZYK

Global Senior Medical Manager, Metabolics
Nutricia Advanced Medical Nutrition

Medical passionate helping patients with inborn errors of metabolism to achieve the best quality of life by early access to neonatal screening and dietary treatment. Enthusiastic leader in education of healthcare professionals in field of dietary management of metabolic diseases and preventions program for PKU patients. Initiator of clinical research in field of IEOM.

PhD in Genetics, Medical University in Lublin, Poland, 1993 doctorate:

Fibronectin gene expression in selected physiological and pathological conditions in gynecology.

Specialist in Gynecology & Obstetrics, Medical Doctor, MD, Diploma with Honors, 1986

20 years of experience in clinical research

17 years of experience in inborn errors of metabolism

- 10 years of experience as an academic teacher
- Over 30 publications, including 9 publications on inborn errors of metabolism
- Regional and local dietary management meetings to build metabolic HCP community in developing countries
- Global educational materials for HCP and patients:
 - Local language versions of TEMPLE tool to facilitate diagnose communication for parents and patients with inborn error of metabolism
 - PKU and RMD calculator & communication platform



REEM AL-SAAD

Ms. Reem Al-Saadi is the Director of Corporate Dietetics and Nutrition department at Hamad Medical Corporation –Qatar and her main interest is the dietary management of metabolic diseases

She completed her bachelor’s degree in Human Nutrition from Qatar University

She joined HMC as general dietitian in 2004 then specialized in pediatric nutrition and subspecialized in the dietary management of Metabolic and Inborn Error of Metabolism diseases in 2006

She got a training course for the dietary management of metabolic diseases at the University of Heidelberg, Germany in 2006

She attended a course in the dietary management of inherited metabolic disorders, London-2008

She got a training course in Ketogenic diet with a well-known expert - Kuwait in 2009

She completed her internship in dietary management of metabolic diseases, then completed International Learner program in inborn errors of metabolism at Sick kids hospital - Toronto - Canada in 2011

She attended a course in Dietetic management of inherited metabolic disorders (Module 4) - Birmingham in 2011

She attended and participated in different courses, conferences and lectures for the new born screening program

She participated and attended most of the national, regional and international metabolic conferences

To be more practical Ms. Reem participated in the development of the metabolic center and initiated the metabolic kitchen at Hamad Medical Corporation and prepared different low protein recipes with demonstrations by inviting and joining different experts from different countries

Annually Ms. Reem conducting the Homocysteinuria family day for Homocysteinuria patients and their families as they are part of the management program

To keep them updated and coping with the most recent guidelines, continuously Ms. Reem hosting experts of different metabolic specialties to make workshops or present lectures for metabolic dietitians at Hamad Medical Corporation , in addition to keep all the health care team members aware about diet , she trains physicians and nurses for the dietary management of metabolic diseases

As she is the most professional metabolic dietitian in Qatar she is representing Hamad Medical Corporation for all the activities related to metabolic nutrition by Conducting and presenting various metabolic workshops and lectures locally, regionally and internationally



ANJA WITTKOWSKI

Dr Anja Wittkowski is a Senior Lecturer/ Associate Professor in Clinical Psychology in the Division of Psychology and Mental Health, School of Health Sciences, at the University of Manchester (UoM). She completed all of her degrees at the University of Manchester and since her graduation as a Doctor in Clinical Psychology in 2001 she has been a research active clinical academic working at this prestigious university. She is also working as a Health and Care Professions Council registered Clinical Psychologist for the Greater Manchester Mental Health NHS Foundation Trust.

Her research interests are closely linked to her clinical work at the national psychiatric, inpatient Mother and Baby Unit at Wythenshawe Hospital in Manchester, England. They centre broadly on antenatal and postpartum psychological mental health difficulties, including postpartum psychosis, postnatal depression and problems in the mother-infant-relationship. At present she is particularly interested in examining the

effectiveness of psychological and parenting interventions in the treatment of women with serious perinatal mental health problems and the impact any improvements may have on the mother-infant-relationship. She is a co-applicant and the Manchester Lead for the National Institute Health Research (NIHR) Public Health Research funded THRIVE trial (Henderson, Wittkowski, et al. 2013-2019; NIHR Public Health Research Programme) and she is the Principal Investigator of a NIHR Research for Patient Benefit funded feasibility study of the Baby Triple P Positive Parenting Programme for mothers with severe mental health problems, called the IMAGINE study (Wittkowski et al., 2016-2019). However, her research interests extend to parenting programmes and the parenting experience more general as well, including the experience of parents whose children have health problems.

She regularly supervises several research assistants as well as PhD and ClinPsyD doctoral students. She has published numerous systematic literature reviews, empirical study papers and she has contributed to some book chapters. Finally, in her academic role she is the Families and Parenting Research Group lead.

For further information, please see: <https://www.research.manchester.ac.uk/portal/anja.wittkowski.html> or <https://www.research.manchester.ac.uk/portal/anja.wittkowski.html>.



OWEN AUSTIN

I’m Owen Austin. I was diagnosed with classical homocystinuria when I was 7 years old.

I am a tough person and have taken this diagnosis by the horns... so people tell me!

I had a lot to learn and more to come with each life stage I hit - however I won’t let it beat me... today I will be speaking about living with classical homocystinuria from a child’s point of view.



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. Judy and Susie passed away due to homocystinuria in the early 1970s and Margie is committed to finding a cure for homocystinuria so that someday no children will suffer like her sisters did, and no families will need to deal with the impact of this devastating illness on their family members or the fear of passing the disease along to additional offspring.

After receiving a BS in Pharmacy and an MBA in Marketing from The University at Buffalo, Margie spent 26 years at Merck where she served in leadership roles in marketing, new product development and managed care, last serving as President, Global Vaccines and Anti-Infectives. After retiring from Merck, Margie served for 4 years as President and Chief Executive Officer of the International AIDS Vaccine Initiative (IAVI), a Product Development Partnership which helps accelerate HIV vaccine development by bridging government and philanthropic funding with academic and industry vaccine research and development capabilities. Margie also serves on the boards of Vertex Pharmaceuticals, Amicus Therapeutics, Orphan Technologies, and Air Products and Chemicals.



ROSSELLA BRINDISI

Rossella Brindisi is the President of the CBLC Onlus and also is the mother of two sons, the second born affected by cobalamin (cbl) C deficiency diagnosed when he was 18 months old.

In March 2017, along with 4 other families in similar situations, the CBLC Onlus association was created, with the purposeful intention to support scientific research and to improve the quality of life of patients and their families. In a short time the association has reached a significant number of Italian families, but also some in Spain and one in California.

Rossella graduated in Economics and received a Master Degree in Tax; she worked in finance & administration and subsequently in the communication field until the birth of the second son; such educational and professional background has been usefully deployed for the organization and management of the association.



LUANA BRITO

Luana Brito is a 35-year-old Brazilian journalist, mother of a child with Methylmalonic Acidemia with Homocystinuria. She's representing cblC Brazil group for the second time at the Patient-Expert Meeting. The group is composed of patient relatives and aims to promote the exchange of information, ideas and experiences among the participants, in order to offer a better quality of life for the patients.

We would like to acknowledge and thank the following companies who have generously sponsored the Third International Homocystinurias Patient – Expert Meeting 2019.

SILVER SPONSORS



Orphan Europe, part of the Recordati Group, is a pharmaceutical company aiming at providing treatment for patients with unmet medical needs suffering from rare diseases. Since 1990, Orphan Europe is established as one of the most active players in the field of rare diseases.

Orphan Europe is committed to the improvement of knowledge about rare diseases among healthcare professionals. The best example is the support of Recordati Rare Diseases Foundation that provides unique, independent and high-level education on rare diseases.

Orphan Europe shares the conviction that every single patient has the right to the best possible treatment.

For more information, please visit www.orphan-europe.com



Orphan Technologies is dedicated to developing novel therapies to dramatically improve the lives of patients suffering from rare disorders. OT-58, our lead drug development candidate, has been optimized as an enzyme replacement therapy for classical homocystinuria, a genetic disease characterized by debilitating cardiovascular, skeletal, neurologic, and ophthalmologic complications. OT-58 is designed to reduce homocysteine levels via a targeted mechanism of action and may have therapeutic

applications in other diseases. For more information, please visit www.orphantechnologies.com.

OT-58, Orphan Technologies' lead drug candidate, is a modified recombinant enzyme replacement therapy in development as an enzyme replacement therapy for patients suffering from the rare disease classical homocystinuria. Classical homocystinuria is a genetic metabolic disease caused by a deficiency in the CBS enzyme leading to elevated levels of the amino acid homocysteine. OT-58 has consistently demonstrated significant reductions in homocysteine levels across multiple models of homocystinuria and has the potential to improve metabolic control, reduce or remove dietary restrictions, and positively impact clinical outcomes. OT-58 is anticipated to enter clinical evaluation in 2018 and has been granted Orphan Status by the US Food and Drug Administration and EMA. In addition, based on its mechanism of action, OT-58 has therapeutic potential in other diseases.

For more information, please visit www.orphantechnologies.com

SILVER SPONSORS (CONTINUED)



Nutricia pioneers nutritional solutions that help people live longer, more joyful and healthier lives.

Building on more than a century of nutritional research and innovation, Nutricia continues to transform lives through the power of nutrition.

Nutricia's science-based products and services support healthy growth and development during the first 1000 days. Nutricia also helps to address some of the world's biggest health

challenges including conditions in early life such as pre-term birth, faltering growth, food allergy and rare metabolic diseases, as well as age-related conditions and chronic disease, such as frailty, cancer, stroke and early Alzheimer's disease.

Nutricia Metabolics is the world's leading metabolic nutrition company supporting the greatest number of people across the widest range of inborn errors of metabolism. We use our unique nutritional expertise to develop high-quality products and services that help make the lives of patients, their families, and the healthcare professionals that support them a little easier.

Our core portfolio includes the leading ranges Anamix, Lophlex and Milupa Metabolics, as well as breakthrough innovations such as PKU Synergy and PKU GMPPro. Nutricia Metabolics provides a wide range of low-protein foods that support patients with amino acid-based inborn errors of metabolism.

In addition to our product portfolio, we provide a range of comprehensive information and support services, including scientific brochures and literature for healthcare professionals, educational tools and recipe brochures for patients and their families.

For more information visit www.nutricia.com

BRONZE SPONSORS



Founded in Genoa in 1915 by Edoardo Maragliano, the man who discovered the first tuberculosis vaccine, PIAM is an Italian pharmaceutical company that has developed its core business in specialist and ethically significant therapeutic areas with prescription drugs.

Over time it has gained particular expertise in hereditary metabolic diseases. In the 70s, PIAM pioneered a specialist nutritional line to support its pharmaceutical products. It is able to offer a complete response for patients with disorders requiring particular nutritional therapy, throughout every phase of their lives.

For more information, please visit www.piamfarmaceutici.com/en/



BioElectron is a platform biotechnology company that is using its expertise in redox chemistry to develop first-in-class therapeutics for CNS and non-CNS diseases characterized by redox defects. BioElectron's lead clinical compound—EPI-743—is in late clinical stage development for mitochondrial disease and related orphan disorders with shared biochemistry, including cobalamin C defect. In addition, BioElectron has a rich pipeline of platform-derived compounds in various stages of development from preclinical to phase 2.

For more information, please visit www.bioelectron.com



VitaFlo are at the forefront of developing innovative specialised clinical nutrition products for Metabolic Disorders such as Homocystinuria and other specific conditions. Our aim is to create products that combine the best of cutting-edge research with the lifestyle demands of modern living, ensuring the most acceptable products are available for the patient. By constantly evolving to meet patient needs, VitaFlo will continue to develop products which offer patients choice and help support them in complying with restrictive therapeutic diets. For more information, please visit www.vitafloweb.com



metaX, works with prestigious universities and special hospitals, research laboratories and competent business partners. metaX offers dietetic Foods for Special Medical Purposes: Protein Supplements, powdered and liquid, a wide range of Low Protein Products for patients with PKU, HCU and many other rare disorders of metabolism, Supplements for Food Fortification, a Micronutrient Supplement System and products for the dietetic management of Chronic Renal Failure.

metaX services include brochures, recipes, cooking classes, holiday activities for patients and medical symposia for professionals. For more information visit www.metax.org

SOCIETY SPONSORS



The aim of the Society of the Study of Inborn Errors of Metabolism is to foster the study of inherited metabolic disorders and related topics. The Society, founded in 1963, exists to promote the exchange of ideas between professional workers in different disciplines who are interested in inherited metabolic disease. Pursuing this aim by arranging scientific meetings, publications and in other ways considered appropriate by the Council. The Council is also supported by advisory council members who provide advice and meet with the Council at the annual symposium.

For more information, please visit www.ssiem.org

SUPPORTERS



Cambrooke Therapeutics (expansion of Cambrooke Foods) was founded in 2000 by Lynn and David Paoella, the parents of two children diagnosed with a rare disease called phenylketonuria (PKU). PKU is one of the few genetic diseases, which is managed almost entirely with nutritional intervention. The Paoellas' goal in forming Cambrooke was simple – to develop improved nutritional therapeutic options for those with serious medical disorders.

For more information, please visit www.cambrooke.com



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CONTRIBUTION AND ATTENDANCE.