PVRI Chronicle

News, Discussions, Science and Medicine from the Pulmonary Vascular Research Institute

Today’s work, tomorrow’s possibility.
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Passing the torch

by Sachindra Joshi

With the current issue, my term as an Editor-in-Chief of the PVRI Chronicle comes to an end. As we move on, I would like to pass the torch to Dr. Eileen Bauer, a young and enthusiastic PVRI fellow, to initiate the new beginnings henceforth.

The founding editor of the PVRI Journal, Dr. Harikrishnan once said “Change is constant and the course of life”. Indeed, PVRI Journal has evolved from PVRI Review to PVRI Chronicle. It has become the brand ambassador of the PVRI in upholding the Institute’s mission statement by focusing on the traditional triad of research, education, and clinical care, in activity and report alike. I am very fortunate to be a part of this progress.

This evolution brought different sections, PVRI News and Activities, Journal Club, Art Club, Learners' Corner and Clinical Corner to accommodate articles from a wide range of areas and perspectives in order to form a truly inclusive view on the state of pulmonary vascular disease and the actions of the PVRI and its members. As journey continues in future issues, I would like to invite new ideas to further improve the journal and serve the institute’s mission in excellence. In this issue, “Team PHenomenal Hope”, one of the articles in PVRI News and Activities certainly brings hope to the pulmonary hypertension community. Team Phenomenal Hope aspires to make impactful differences in the lives of people with pulmonary hypertension by educating and bringing awareness about the disease as well as inspire others to rally to this cause through fundraising and awareness campaign. I would like congratulate Dr. Patricia George, President of Team PHenomenal Hope for such a noble initiative and echo for the action from PVRI community to race as a Team PH.

In PVRI News and Activities, Michael Seimetz and Mario Boehm succinctly summarized the Annual Congress of the European Respiratory Society (ERS) that took place in Amsterdam from 26-30th September 2015. In addition, Prof. Ghazwan and Talent Sooronbaev reported the activities of the PVRI Central Asia Task force, now Central Asia Pulmonary Hypertension (CAPH) group. In the Journal Club, we have selected three interactive discussions: Pulmonary arterial hypertension and aging: Is there a connection?; Hypoxic pulmonary hypertension: hypoxic pulmonary vasoconstriction vs. vascular remodeling; and E-cigarettes: A fairy tale of a healthy alternative to conventional cigarettes?. In the art club, current infographic illustrates prevalence and hospital discharge status of human immunodeficiency virus–associated pulmonary arterial hypertension in the United States. The Learners’ Corner presents a review article on Pulmonary hypertension in Constrictive Pericarditis or Systemic Lupus Erythematosus patients?; Interview with Dr. Buddha Basnyat: High altitude physiology and medicine and potentiality of conducting high altitude research in Nepal and a Did You Know article “Secret anchors in the cell – tetraspanins”. The Clinical Corner presents an interesting case report on Upfront dual combination therapy in a patient with polymyositis complicated by pulmonary hypertension; an Interview: Pulmonary Arterial Hypertension Associated with Scleroderma: The Patient’s Perspective; and a original research article in Russian language on: Evaluation in Postoperative Period of Children with Pulmonary Arterial Hypertension.

Editing and putting together the international journal takes enormous amount of time and dedication. I thoroughly enjoyed the editorial task, especially creatively designing PVRI Chronicle and its cover page cartoon. The opportunity of reviewing articles from the authors and communicating with PVRI fellows around the globe to collect feedbacks and make editorial decisions is in itself a reward and indeed of greatest satisfaction. Having said that, leading journal is a team work and I cannot thank enough to my fellow editors and the PVRI fellows who directly and indirectly helped me bring out...
the best in PVRI journals. I would like to specially thank Prof. Ghazwan for his vision and providing me with this opportunity. Also, Nikki Krol, our past Executive editor of PVRI Journal (PVRI Review and PVRI Chronicle) equally deserves my sincere gratitude. She was a life-blood of PVRI. Finally, I would like to express my greatest thanks to the current Editorial Board members and CYCS members for their continuous support and help. Please join me in welcoming our new Editor-In-Chief, Dr. Eileen Bauer as I pass on the torch.
Programme // Rome 2016

10th PVRI Annual World Congress on Pulmonary Vascular Disease
Our Belief.

Why do we exist as an organisation? Our belief is that we are only able to do what we do because of collaboration.

What does collaboration mean to us? Collaboration means trusting someone else to have more valuable input than yourself.

How do we create this collaboration? We create a forum for people to build this trust. Our members challenge each other, they learn from one another and the conversations they have change the shape of the medical industry together.

PVRI members Our members range from post-doctoral students to the world’s leading scientists and clinicians. This holistic perspective is unique to us as an organisation and one we are most proud of.

A global profile The result of this ethos is globally raising the profile of Pulmonary Vascular Disease (PVD), facilitating the research of PVD and encouraging the development of new medicines.

Through global collaboration, we make today’s work tomorrow’s possibility.
Welcome to our Annual World Congress 2016

It gives me great pleasure to welcome you to Italy, a country where it is said all roads lead to Rome, and thus it is in Rome that we meet.

The scientific and cultural programmes look fantastic and grateful thanks are due to Dario Vizza, Stefano Ghio, Kurt Stenmark and Glennis Haworth for their hard work in organising the scientific part of the meeting.

The sessions on imaging, novel targets for therapy and Eisenmenger syndrome look particularly informative and are guaranteed to provide a rich basis for debate.

I would like to make the specific point that unlike many scientific meetings which seem to have lost the energy for robust debate, the PVRI retains that characteristic and Rome provides the perfect backdrop for gladiatorial combat as in days gone by at the Colosseum!

Thanks also to Andrea Rich, Stephanie Barwick and Aaron Shefras for their invaluable work in organising the venue, the sightseeing tours and the Gala Dinner. These things don’t occur by chance and we are fortunate that so many people work so hard on behalf of the PVRI.

We look forward then to a wonderful spectacle and the opportunity to advance our understanding of the pathobiology and treatment of PAH, of benefit to patients all over the globe with this disease.

We hope you enjoy our Annual Congress in Rome which brings our members together from all over the world.
“...we look forward to active delegate participation and some heated debates in our open forum style sessions!”

Our Speakers, Chairs & Commentators
Introduction...

I am delighted to introduce you to our speakers, chairs and commentators, who include the most distinguished leaders in the field of pulmonary vascular disease. I would like to thank everyone for their contributions and participation in our event.

Our speakers, chairs and commentators come from all over the world. Together they represent 18 different countries, including Europe, North and South America, the Middle East, India and China. Being the only global charity involved in pulmonary vascular disease, we are immensely proud of our international reach.

The presentations and contributions on offer will bring a unique perspective from the latest advancements in scientific research to practical experiences from the developing world, which should give plenty of food for thought, active participation and lively debate.

As is tradition in the PVRI meetings, we have left plenty of room for discussion during our networking cocktail reception on Thursday evening or the free afternoons.

Stephanie Barwick
Chief Executive Officer
Canterbury, UK

Our Speakers, Chairs & Commentators LISTED IN ALPHABETICAL ORDER

Ian Adatia
MD, PhD

Ian Adatia is a Professor of Paediatrics at the University of Alberta, Director of the Paediatric Pulmonary Hypertension Service and a Paediatric Cardiac Intensivist at the Stollery Children’s Hospital and Mazankowski Alberta Heart Institute, Edmonton, Canada.

He completed his medical degree at Bristol University, England in 1980 and undertook his pre-registration house jobs at Ballochmyle Hospital, Scotland and Addenbrooke’s Hospital, Cambridge, England. He worked at West Cumberland Hospital, Whitehaven, England and Caithness Central Hospital, Wick, Scotland, before training in paediatrics at Raigmore Hospital, Inverness, Scotland and the Stollery Children’s Hospital, Edmonton, Canada. He took time out to travel for 18 months in Central America, Asia and Eastern Europe.

Dr. Adatia trained in paediatric cardiology at the Toronto Hospital for Sick Children, Canada, paediatric cardiology intensive care at Boston Children’s Hospital, USA and paediatric pulmonary vascular disease at Great Ormond St Hospital for Sick Children and at University College London, UK. He has held staff positions at Freiburg Children’s Hospital, Germany, as well as at Boston Children’s Hospital, USA and Toronto Hospital for Sick Children, Canada, and University of California San Francisco Children’s Hospital, USA. Dr. Adatia’s clinical and research interests include perinatal care of children with congenital heart disease and disorders of the pulmonary vascular bed.

In addition, he has published 25 book chapters, 100 abstracts and 108 peer-reviewed papers. He co-organises, with Jeff Fireman, the International Conference on Neonatal and Childhood Pulmonary Vascular Disease held in San Francisco each year.

Stephen Archer
MD, PhD

Dr. Archer, born in Canada, is a graduate of Queen’s University, Kingston, Ontario.

After interning at the Royal Columbian Hospital in New Westminster, British Columbia, he completed training in Medicine and Cardiology at the University of Minnesota. He worked at the Minneapolis VA Medical Center from 1988-97, attaining the rank of Professor of Medicine.

From 1998-2007, he served as Professor of Medicine and Physiology and Director of the Cardiology Division at the University of Alberta.

In April 2007, he became Chief of the Cardiology Section of the University of Chicago and Harold Hines Jr. Professor of Medicine. He is currently Professor and Head of Medicine at Queen’s University.

Dr. Archer’s current research, funded by NIH and NHLBI, focuses on defining the role of mitochondrial fission/fusion and metabolism in oxygen-sensing/cell proliferation and translating this into pulmonary hypertension and cancer therapies. He is currently a Tier 1 Canada Research Chair in Mitochondrial Dynamics and Translational Medicine. He has published over 230 publications with 23,000 citations. His research is published in journals such as The New England Journal of Medicine, The Lancet, Circulation, Cancer Cell, the Proceedings of the National Academy of Sciences and Circulation Research.

Dr. Archer has delivered numerous named lectureships in North America, Europe and Asia, including plenary session lectures at the American Heart Association (AHA) meeting. He has also been an author of several key guideline documents, including the AHA 2009 guidelines on pulmonary hypertension and the 2010 guidelines on management of submassive veno-occlusive disease.

Joan Albert Barberà
MD, PhD

Joan Albert Barberà achieved his academic degrees at the University of Barcelona and completed his scientific training in the Pulmonary Research Laboratory at the University of British Columbia, Vancouver, Canada, under the direction of Prof. JC Hogg.

Dr. Barberà is Senior Consultant of the Department of Respiratory Medicine, Hospital Clinic, University of Barcelona and Head of the Pulmonary Hypertension Unit. He is Expert Panel Member of the 3rd (Venice 2003), 4th (Dana-Point 2008) and 5th (Nice 2013) editions of the World Symposium on Pulmonary Hypertension as well as a Member of the Task Force that prepared the European Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension, endorsed by the European Respiratory Society and the European Society of Cardiology. He is Co-chair of the Consensus Document on Standards of Care in Pulmonary Hypertension, endorsed by the Spanish Societies of Pulmonology and Cardiology.

He is author or co-author of more than 200 research articles published in peer-reviewed journals, including N Engl J Med, Lancet, Ann Intern Med, Am J Respir Crit Care Med, Circulation, Thorax, Eur Respir J and Cardiovasc Res. His research interests are currently focused on the mechanisms of pulmonary vascular remodelling and endothelial dysfunction in the pulmonary circulation, both at cellular and molecular levels, particularly in COPD and the identification of biomarkers that might serve to track pulmonary vascular changes.

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Dr. Barberà is Senior Consultant of the Department of Respiratory Medicine, Hospital Clinic, University of Barcelona and Head of the Pulmonary Hypertension Unit. He is Expert Panel Member of the 3rd (Venice 2003), 4th (Dana-Point 2008) and 5th (Nice 2013) editions of the World Symposium on Pulmonary Hypertension as well as a Member of the Task Force that prepared the European Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension, endorsed by the European Respiratory Society and the European Society of Cardiology. He is Co-chair of the Consensus Document on Standards of Care in Pulmonary Hypertension, endorsed by the Spanish Societies of Pulmonology and Cardiology.

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Maria Angelica Binotto
MD, PhD
Maria Angelica Binotto is a Paediatric Cardiologist, Heart Institute (InCor), University of São Paulo Medical School, Director of the Fellowship Programme in Paediatric Cardiology, University of São Paulo Medical School and President of the Paediatric Cardiology Department, Brazilian Society of Cardiology (2016-2017).

Dr. Binotto is also a fellow of the Pulmonary Vascular Research Institute (PVRI) and member of the Paediatric and Congenital Heart Disease Task Force, PVRI.

Damien Bonnet
Damien Bonnet is head of the Congenital and Paediatric Cardiology Department at Necker Hospital.

He coordinates the national reference center for complex congenital heart diseases - MJC - as well as the French reference centers for paediatric pulmonary hypertension and inherited heart diseases.

His main fields of interest are development and genetics of congenital heart diseases in close link with innovative treatments of long term sequelae such as chronic cardiac failure and pulmonary hypertension.

Damien Bonnet has been involved in numerous therapeutic trials in pediatric pulmonary hypertension as well as in registries in the field.

Furthermore, he has proposed using the Potts shunt as an alternative to lung transplantation in severe paediatric pulmonary hypertension.

Paul A. Corris MD
Paul Corris is Professor of Thoracic Medicine and is a tenured faculty member of the Institute of Cellular Medicine at Newcastle University. He is an Honorary consultant physician at The Newcastle Hospitals NHS Foundation Trust Newcastle upon Tyne, UK, and directs the National Pulmonary Vascular Service (Newcastle).

He is Deputy Director of the Transplant Institute within the Institute of Cellular Medicine at Newcastle University and is Past-President of both the British Thoracic Society and the International Society for Heart and Lung Transplantation. In 2014, he was elected President Elect of the international Pulmonary Vascular Research Institute and is currently chairman of NHS England Clinical Reference Group for Pulmonary Hypertension.

Professor Corris played significant roles in establishing lung transplantation as a viable clinical therapy for patients with end-stage lung disease internationally, and in setting up the UK National Pulmonary Hypertension Service collaborative. He currently sits on the editorial boards of Pulmonary Circulation, Frontiers in Pulmonary Medicine and the Journal of Heart and Lung Transplantation.

Previously, he was Associate Editor of Thorax and is the author of 275 peer reviewed manuscripts and 60 book chapters. He has been a faculty member and author of guidelines within his specialty interests of lung transplantation and pulmonary hypertension for many societies and world groups. His research has been highly cited and is focused on translational and clinical science relating to both Lung Transplantation and Pulmonary Hypertension. His interests outside medical science include wine, music, mountains and sport, particularly rugby and soccer.

Maria Jesus del Cerro Marin MD PhD
Maria Jesus del Cerro Marin graduated in medicine in 1987 in Madrid and in 1997 completed a PhD in Thyroid function alterations in children with congenital cardiac disease after catheterisation with iodinated contrast agents.

From 1992 to date she has been part of the Paediatric Cardiology Unit of La Paz Hospital, working in the field of Interventional catheterisation and Pulmonary Hypertension. From 2006 to 2013 she was Head of the Paediatric Pulmonary Hypertension Unit at La Paz and since 2013 has been Head of the Paediatric Pulmonary Hypertension Unit at Ramon y Cajal University Hospital.

Since 2008 she has been President of the Working Group on Pulmonary Circulation of the Spanish Paediatric Cardiology and Congenital Heart Disease Society.

She is head of the Spanish Register of Paediatric Pulmonary Hypertension (REHIPED) and co-leader of the Paediatric Task-Force of the PVRI.

Her particular areas of interest are paediatric pulmonary hypertension and diagnostic and interventional catheterisation.

Michele D’Alto
MD PhD FESC
Michele D’Alto is Professor at the School of Cardiology, Second University of Naples, and Consultant Cardiologist and Chief of the Pulmonary Hypertension Unit at the Department of Cardiology at Monaldi Hospital, Naples, Italy.

Professor D’Alto is a member of the European Society of Cardiology, the Italian Society of Cardiology and the Italian Society of Cardiovascular Echocardiography.

He has trained in invasive cardiology and electrophysiology and his research and clinical interests are mainly focused on pulmonary hypertension, congenital heart diseases, cardiac arrhythmias and echocardiography.

Professor D’Alto has published eight book chapters on Cardiology and more than 70 papers in peer-reviewed international journals (45 in the last five years), mainly focused on pulmonary hypertension. He is a reviewer for major cardiovascular journals and regularly lectures at national and international centres.

In addition, he has been involved as principal investigator in numerous clinical trials in the field of pulmonary arterial hypertension.
Andrea D’Armini
Andrea Maria D’Armini is Professor of Cardiac Surgery at the University of Pavia School of Medicine, Foundation I.R.C.C.S. Policlinico San Matteo, Pavia, Italy, where he is also Director of the Cardiac Surgery Residency School and Head of the Unit of Thoracic Transplantation and Pulmonary Hypertension. His surgical expertise includes pulmonary endarterectomy, heart transplants, isolated lung transplants, and heart-lung transplants. Professor D’Armini has been the Principal Investigator on several clinical trials investigating the medical treatment of pulmonary hypertension. He is a member of a number of scientific societies and has authored or co-authored more than 120 PubMed-indexed publications.

Pilar Escribano-Subias
Pilar Escribano Subias received her MD from the University of Zaragoza, Spain, and her PhD from the University Complutense of Madrid. She has several publications in the field. In her daily practice, Dr Escribano has experience with patients with pulmonary hypertension in heart failure and adults with congenital heart disease, and has a strong interest in clinical studies and new clinical applications in these areas. Other interests include the epidemiology of pulmonary hypertension and the utility of different diagnostic tools. She has served as President of the Pulmonary Circulation Group for the Spanish Society of Cardiology (SEC) and is SEC Coordinator for the National Registry of Pulmonary Arterial Hypertension (REHAP) initiated by SEC and the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR).

Sean Gaine
MB PhD FRCP FESC
Professor Sean Gaine is Consultant Respiratory Physician at Mater Misericordiae University Hospital in Dublin and Director of the National Pulmonary Hypertension Unit. He completed his medical education at Trinity College Dublin and his medical residency and fellowship training at the Johns Hopkins Hospital, Baltimore. During his Pulmonary and Critical Care fellowship, Professor Gaine obtained his PhD for work exploring the control of pulmonary vasculature function. He subsequently held faculty positions at the Johns Hopkins Hospital and at the University Of Maryland School Of Medicine. He established the Pulmonary Hypertension Center at the Johns Hopkins Hospital in 1999 and subsequently the National Pulmonary Hypertension Unit upon his return to Dublin. His research interests include novel biomarkers and new therapeutic agents in pulmonary vascular diseases. Professor Gaine has been a working member of the European Society of Cardiology and European Respiratory Society guidelines committee on Pulmonary Hypertension in the past and a task force member of the WHO World PH symposiums since 2003. He is a member of numerous international associations, and a fellow of the College of Chest Physicians, the Royal College of Physicians in Ireland and the Faculty of Sports and Exercise Medicine. He is Chief Medical Officer of the Olympic Council of Ireland and led the medical team at the Olympic Games in Athens, Beijing and London.

Stefano Ghio
MD FESC
Dr. Stefano Ghio obtained his medical degree (cum laude) from the University of Pavia School of Medicine aged 23 years-old, in 1982 and specialised in Cardiology at the University of Pavia School of Medicine, Pavia in 1987. Since then, he has been working in the Division of Cardiology of Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, Currently, he is Head of the Heart Failure and Pulmonary Hypertension Unit. Dr. Ghio has authored or co-authored over 140 papers in indexed medical journals on topics that include pulmonary hypertension, cardiac resynchronisation therapy, cardiac imaging techniques in heart failure and cardiomyopathies. He has been fellow of the European Society of Cardiology since 1991.

Hossein Ardestchi Ghofrani
MD
Hossein A. Ghofrani is Professor of Pulmonary Vascular Research at Justus Liebig University, Giessen, Germany and Head of the Pulmonary Hypertension Division at the University Hospital in Giessen.

In addition, he is Director of Pneumology as well as Medical Executive Director at the Kerckhoff Clinic in Bad Nauheim, Germany and part-time Professor for Pulmonary Vascular Medicine at Imperial College London. He leads a translational research group on development of new therapeutics for Cardiopulmonary Vascular disease and is member of the steering committee of the Excellence Cluster Cardio-Pulmonary System (www.ecps.de) and founding member of the Pulmonary Vascular Research Institute (www.pvri.info). He has participated in the development of several therapeutics for chronic lung diseases and pulmonary hypertension, including prostanoids, phosphodiesterase inhibitors, endothelin receptor antagonists, tyrosine kinase inhibitors and stimulators of the soluble guanylate cyclase. Professor Ghofrani has received four awards for investigations in pulmonary vascular science, is a fellow of the European Respiratory Society (ERS) and reviewer for several medical scientific journals.
She became Professor of Developmental Cardiology at Great Ormond Street Hospital for Children and had a British Heart Foundation (BHF) Professorial Chair and research group. Her basic science focussed on the pathophysiology of paediatric pulmonary hypertension and adaptation of the pulmonary circulation to extra-uterine life. Professor Haworth was Head of Cardiorespiratory Sciences at the Institute of Child Health, University College London. In 2002 she founded the UK Pulmonary Hypertension Service for Children, a comprehensive clinical network caring for all children in the UK with significant pulmonary hypertension. She has published extensively and helped train pulmonary hypertension specialists who are now leaders in the field. Professor Haworth has served on the BHF Executive Committee and the BHF Research Fund Committee, working groups of the Royal Colleges; Selection Committee of the Academy of Medical Sciences, London; and became a fellow of the American College of Cardiology and a member of the Cardiac-Pulmonary Committee of the American Heart Association. She was a member of the Fullbright Selection Committee in London, has acted as an expert advisor in medico-legal litigation, served on pharmaceutical advisory boards, and is a Patron of the Pulmonary Hypertension Association UK. Throughout her career Professor Haworth has travelled widely, trying to help those working in difficult circumstances, particularly in India where she has worked since 1975. Professor Haworth has been a strong supporter of the PVRI since its inception and has been particularly concerned to further the interests of those working in developing countries.

**Marco Guazzi**
MD, PhD, ACC, FAHA, IRCSS
Marco Guazzi is a Professor of Cardiology at the University of Milano and Head of the University Department of Cardiology at IRCSS San Donato University Hospital, Milan.

His research primarily focuses on the pathophysiological and prognostic insights of heart failure syndrome and Group 2 PH. He has established several clinical research programmes involving HF functional evaluation, therapy and pulmonary vascular disease.

Between 2005 and 2007 he served as Chair of the Exercise Physiology and Rehabilitation Working Group of the Italian Society of Cardiology. Currently, he is on the Board of Nucleus of the Exercise and Translational Physiology Group of the European Society of Cardiology. Professor Guazzi serves on the Editorial Board of the Journal of Cardiac Failure; he is Associate Editor of the European Journal of Prevention and is the author or co-author of over 300 manuscripts.

**Paul Hassoun MD**
Dr. Paul Hassoun is a paediatric cardiologist and development worker from Bolivia.

Having been trained in paediatric cardiology at the University Hospital of Aachen, his work has since focused on the treatment of indigenous children from the Andes region at 4,000 m above sea level with congenital heart disease prevalence of 2 per cent. The inauguration of her clinic, Kardiozentrum and the Bolivian Ministry of Health, Alliances with hospitals in rural areas of the country have permitted her to reach the most remote regions of the country, hence obtaining a significant and unprecedented database on congenital heart disease prevalence in the highlands.

Dr. Hassoun has published extensively on the subject of congenital heart disease at high altitude and has shown particular interest in the relation of high altitude and pulmonary hypertension as well the deployment of transcatheter closure of large patent ductus arteriosus. She graduated with honours from Universidad Mayor de San Andrés (La Paz) and holds an MD from Ludwig Maximilian University in Munich, Germany.

**Alexandra Heath PhD**
Dr. Heath is a paediatric cardiologist and development worker from Bolivia.

She is a translational physician-scientist with a research focus on the role of altered metabolism in pulmonary vascular disease. Her basic research is on the effect of BMP2 mutation on insulin-mediated intracellular signaling in the pulmonary vasculature and the right ventricle. Clinical research interests have focused on insulin resistance and metabolic syndrome in human pulmonary vascular disease with a focus on genetic susceptibility to these conditions. Additionally, Dr. Heath actively sees patients in the Vanderbilt Center for Pulmonary Vascular Disease and has effectively used this population to recruit into clinical studies for pulmonary vascular disease, including the treatment of pulmonary hypertension and diagnostic modalities in pulmonary vascular disease. This provides a unique and powerful capacity to study molecular mechanisms of pulmonary vascular disease and right heart dysfunction in studies spanning cell culture and rodent models through human translational studies and clinical trials.

Dr. Heath is the author or co-author of over 70 articles in peer-reviewed publications. Also, she is a Member of the: American Thoracic Society; Chest Foundation; American Heart Association; Pulmonary Hypertension Association; and Chair-Elect, Program Committee, Pulmonary Circulation Assembly, American Thoracic Society.
Our Speakers, Chairs & Commentators  LISTED IN ALPHABETICAL ORDER

Majdy Idrees
Dr. Idrees is Formal Head of the Pulmonary Division at Riyadh Armed Forces Hospital, Director of the Pulmonary Vascular Disease Unit and Head of the Saudi Association for Pulmonary Hypertension.

He received his M.B. B.S. degree from King Saud University in Riyadh, Saudi Arabia, and completed his postgraduate training in both Internal Medicine and Pulmonary Medicine at The University of British Columbia, Canada from 1992 - 1997. He gained his American Board degree in Pulmonary Medicine in 1996, and the Canadian Board degree in Pulmonary Medicine, 1997. His major area of research is related to pulmonary hypertension and pulmonary vascular diseases and bronchial asthma. He has more than 50 publications in peer-reviewed journals that include book chapters, original papers, and review articles. He is the primary author of the Saudi Guidelines for the management of Pulmonary Hypertension and a co-author for the Saudi Guidelines in both Asthma and COPD.

He is a manuscript reviewer and co-editor of numerous medical journals. Dr. Idrees has been invited as a guest speaker at many more than 350 lectures in different fields of pulmonary medicine.

Donald E. Ingber
MD, PHD

Donald Ingber is the Founding Director of the Wyss Institute for Biologically Inspired Engineering at Harvard University, the Judah Folkman Professor of Vascular Biology at Harvard Medical School and Boston Children’s Hospital, and Professor of Bioengineering at the Harvard School of Engineering and Applied Sciences. He received his B.A., M.A., M.Phil, M.D. and Ph.D. from Yale University.

He is a pioneer in the field of biologically inspired engineering and, at the Wyss Institute: Dr. Ingber leads a multifaceted effort to develop advanced bio-inspired technologies for healthcare and to improve sustainability. In addition, he has made major contributions to mechanobiology, angiogenesis, tissue engineering, cancer research, systems biology, nanobiotechnology and translational medicine. Dr. Ingber has authored more than 400 publications and 100 patents, founded four companies, presented more than 450 presentations worldwide and received numerous honors, including membership in both the U.S. National Academy of Medicine and the American Institute for Medical and Biological Engineering.

Dr. Ingber’s most recent innovation is the development of Organ-on-Chips created with microchip manufacturing methods and lined with living human cells, which are used to replace animal testing for drug development. His Organ-on-Chips technology was recently named both the 2015 Product of the Year and the 2015 Design of the Year by the London Design Museum, and was acquired by the Museum of Modern Art (MoMA) in New York City for its permanent collection.

David G Kiley

David Kiley is a respiratory physician and an Honorary Professor of Pulmonary Vascular Medicine at the University of Sheffield, UK.

He is Chair of the UK and Ireland Pulmonary Hypertension Physicians Committee and a Board Member of the International Workshop on Pulmonary Functional Imaging. David Kiley was appointed as the Director of the Sheffield Pulmonary Vascular Disease Unit in 2001. The Sheffield centre evaluates, each year, over 700 new patient referrals with suspected severe pulmonary hypertension using an approach based on multi-modality imaging including MRI: it is home to the ASPIRE Registry.

David Kiley’s major clinical interests are pulmonary hypertension, pulmonary embolism and respiratory complications of multisystem diseases and he takes part in specialist clinics and the in-patient care of these patients. He participates in a number of research studies funded by the NIHR, MRC and BHF, and his research is primarily focussed on the assessment and classification of pulmonary hypertension with a focus on imaging. In addition, he is heading the PVRI Task force on Imaging in Pulmonary Hypertension and would be grateful if any PVRI members wishing to participate could give their details to the PVRI secretariat.

Krishna Kumar
MD, DM, FAHA

Dr. Krishna Kumar is Clinical Professor and Head of the Department of Paediatric Cardiology at the Amrita Institute of Medical Sciences and Research Center, Cochin.

She has two children aged 4 and 7. Since 2012, with a thesis entitled ‘Non-invasive evaluation, therapy and transplantation in children with pulmonary hypertension’. Her MD thesis investigated changes in the myocardial myosin isoenzyme expression pattern and other adaptational changes induced by hypoxia in an animal model.

From 2000-2004 she trained clinically in paediatric cardiology at the German Heart Centre in Munich and between 2004-2011 worked in London at Great Ormond Street Hospital for Children and the Royal Brompton Hospital in the Cardiology Department and Intensive Care Unit, as a fellow in the Cardiac Transplantation and Heart Failure Team. In addition, she was a fellow and later a Consultant for the UK Pulmonary Hypertension Service for Children. Astrid Lammers received her postgraduate MD (Res) from the University College London in 2012, with a thesis entitled "Non-invasive evaluation, therapy and transplantation in children with pulmonary hypertension."

She participated in PH trials and is involved with safety monitoring of advanced therapy use in children.

She is an active member of the Germany PH Working group as well as European PH Network, fellow of the PVRI and has published several articles about the clinical management and risk predictors in paediatric PH.

Astrid Lammers
MD

Astrid Lammers graduated in 1999 from Hannover Medical School, Germany, where she developed her first interest in pulmonary hypertension.
Allan Lawrie PhD
Allan Lawrie is a British Heart Foundation Senior Basic Science Research fellow in the Department of Infection, Immunity & Cardiovascular Disease at the University of Sheffield.

After obtaining his PhD studying ultrasound mediated gene delivery in vascular cells, Allan Lawrie performed his post-doctoral studies at Stanford University and under the mentorship of Marlene Rabinovich he developed a keen interest in the molecular mechanisms of pulmonary arterial hypertension. He subsequently obtained Independent fellowship funding to returning to Sheffield in 2005. His research has led to prestigious fellowship awards, including a Medical Research Council Career Development Award in 2008 and, most recently, a British Heart Foundation Senior Medical Research Council Career Prestigious fellowship awards, including a to Sheffield in 2005. His research has led to independent fellowship funding to returning hypertension. He subsequently obtained mechanisms of pulmonary arterial developed a keen interest in the molecular Atherosclerosis Society acknowledgement of his research. John French Lecture in 2013 in investigations and publications related to pulmonary vascular disease in the paediatric population and associated with congenital heart disease (children and adults). His particular interest is in microvascular dysfunction markers (endothelial and platelet markers) and mediators of inflammation in pulmonary arterial hypertension (paediatric and adults).

He is fellow of the Pulmonary Vascular Research Institute and member of the Paediatric and Congenital Heart Disease Taskforce. He is also Associate Editor of Pulmonary Circulation. In addition, fellow of the American Heart Association, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation and International Advisor to the Saudi Association for Pulmonary Hypertension - Paediatric and Congenital Heart Disease Taskforce. His research work focuses mainly on translational medicine.

Antonio Augusto Lopes M.D., Ph.D.
Antonio Augusto Lopes is Professor of Medicine (Cardiology) at the Heart Institute (InCor), University of São Paulo School of Medicine, São Paulo, Brazil and Professor of Biostatistics at the University of São Paulo.

He is fellow of the Pulmonary Vascular Research Institute and member of the Paediatric and Congenital Heart Disease Taskforce. He is also Associate Editor of Pulmonary Circulation. In addition, fellow of the American Heart Association, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation and International Advisor to the Saudi Association for Pulmonary Hypertension - Paediatric and Congenital Heart Disease Taskforce. His research work focuses mainly on translational medicine.

Mandy Maclean BSc (1st Class), MBE, FRSE, PhD, FSB, FBPhS.
Mandy Maclean is Professor of Pulmonary Pharmacology, Institute of Cardiovascular and Medical Sciences, College of Medical, Veterinary and Life Sciences, University of Glasgow, Scotland.

Her research has focused on the role of serotonin in the development of pulmonary arterial hypertension (PAH) and more recently her work has concentrated on gender effects and interactions between serotonin and oestrogen metabolism in PAH. Awards include a Royal Society Wolfson Research Merit Award in 2010 and she delivered the prestigious 2008 Estelle Grover Lecture at the ATS Grover conference. In 2013 she was elected as a fellow of The Royal Society of Edinburgh (FRSE), was awarded the British Atherosclerosis Society Astragalus Prize for Women in Pharmacology and a Royal Society Unilever Trust Senior research fellowship. She was Vice President (Meetings) of the British Pharmacological Society from 2007-2009 and currently a member of the MRC Non-Clinical Training Panel, the BBSRC Industrial Case Awardment Panel and the BBSRC Skills and Careers Committee, having just chaired the BBSRC Fellowship review. Professor Maclean is currently a member of the ATS Pulmonary Circulation Assembly Planning Committee. She received an MBE in the 2010 Queen’s New Year Honours list for her career and public engagement activities. Mandy Maclean has always had a passion for postgraduate student training, having attracted over £4m for PhD and MRes opportunities and was appointed College Dean of Graduate Studies from 2010-2013. She also attracted and directed a £3m initiative to build capacity in in vivo skills which was funded by Pharma, UK Research Councils and HEI Funding Councils. She holds advisory roles for in vivo science for the BBSRC, MRC and BPS and has just been elected as an ordinary member of Council for the Royal Society of Edinburgh.

Eleanor Lopez, M.D.
Antonio Augusto Lopez is Professor of Medicine (Cardiology) at the Heart Institute (InCor), University of São Paulo School of Medicine, São Paulo, Brazil and Professor of Biostatistics at the University of São Paulo.

Bradley Maron is an Assistant Professor of Medicine at Harvard Medical School, Associate Physician in the Division of Cardiovascular Medicine at Brigham and Women’s Hospital and Co-director of the Pulmonary Vascular Disease Center at the Boston VA Healthcare System.

His laboratory focuses on developing novel therapeutic strategies for PAH based on the pathogenesis of the disease. His laboratory currently has three main research focus areas: inflammation, mitochondrial biology, and vasoproliferative disease. His research on inflammation has led to the identification of novel targets for PAH treatment. His research on mitochondrial biology has led to the identification of novel targets for PAH treatment. His research on vasoproliferative disease has led to the identification of novel targets for PAH treatment.

Dr. Maron has been an active member of the Pulmonary Vascular Research Institute (PVRI) and has contributed to the advancement of the field of Pulmonary Hypertension. He is a fellow of the Canadian Academies of Health Sciences and a Canada Research Chair (Tier 1) in Applied Molecular and Mitochondrial Medicine. His research is focused on the role of mitochondria and metabolism in diverse diseases like pulmonary hypertension, heart failure and cancer.

Dr. Maron has translated his findings in early phase clinical trials on several occasions. He has been a founding member of PVRi, Ean and Miles Shore Scholar in Medicine and Cardiology at the University of Texas (Galveston), Yale University and University of Minnesota.

He has been at the University of Alberta since 1998 where he is now the Vice Chair (research) of the Department of Medicine. He is a fellow of the Canadian Academies of Health Sciences and a Canada Research Chair (Tier 1) in Applied Molecular and Mitochondrial Medicine. His research is focused on the role of mitochondria and metabolism in diverse diseases like pulmonary hypertension, heart failure and cancer.

Dr. Michelakis has also received numerous awards and honors such as the distinguished Eleanor and Miles Shore Scholar in Medicine and the Harvard Medical School Excellence in Teaching award.

Evangelos Michelakis is Professor at the Medical School, University of Patras and went on to complete his training in vascular biology at the Internal Medicine and Cardiology at the University of Texas (Galveston), Yale University and University of Minnesota.
Our Speakers, Chairs & Commentators LISTED IN ALPHABETICAL ORDER

Shahin Moledina
Dr. Moledina trained as a paediatric cardiologist at both the Royal Brompton and Great Ormond Street hospitals, London.

Nick Morrell
MD FRCP MedSci
Nick Morrell qualified in Medicine (MB BS) from Charing Cross and Westminster Medical School (now Imperial College, London) in 1987.

He undertook his research MD at Charing Cross Hospital and then spent two years in Denver, Colorado, as a British Heart Foundation fellow before returning as a Lecturer to complete training in General and Respiratory Medicine at the Royal Postgraduate Medical School. Hammersmith Hospital (now part of Imperial College School of Medicine). He was appointed Senior Lecturer and Honorary Consultant at Hammersmith Hospital, Imperial College in 1998 and was awarded an MRC Clinician Scientist Fellowship. He moved to the University of Cambridge in 2000 as University Lecturer and Honorary Consultant at Addenbrooke’s and Papworth Hospitals, and was appointed Professor of Cardiopulmonary Medicine in 2007.

In 2009 he was awarded a British Heart Foundation Professorship and in 2011 elected to the fellowship of the Academy of Medical Sciences of the UK. He has chaired the programme committees for the British and American Thoracic Societies. He is a member of the MRC Clinical Fellowships Committee, Director of the BHF Cambridge Centre for Cardiovascular Research Excellence and leads the Cardiovascular Theme of the NIHR Cambridge Biomedical Research Centre. He is Research Director of the National Pulmonary Vascular Diseases Unit at Papworth Hospital and a National Institute of Health Research Senior Investigator. His research focuses on understanding genetic causes of cardiovascular disease, particularly pulmonary arterial hypertension, and developing new treatments for these conditions. He has published over 200 papers in this field.

More recently he has been involved in exciting new genomics initiatives in the UK to apply whole genome sequencing to understanding the genetic basis of rare diseases, including pulmonary arterial hypertension, and to apply this technology to the direct care of patients.

Robert Naeije
MD, PhD
Robert Naeije is Professor Emeritus at the Free University of Brussels (Université Libre de Bruxelles, ULB) and Consultant at the Pulmonary Hypertension Clinic of the Department of Cardiology, Erasme University Hospital, Brussels.

Dr. Naeije gained his MD in 1973 and specialised in Internal Medicine. From 1978 to 1996 he was active as a critical care physician and in 1996 took the Chair of Pathophysiology at the Faculty of Medicine at ULB and founded a Pulmonary Hypertension Clinic at the Erasme University Hospital.

He has published extensively about pulmonary circulation, gas exchange, right ventricular function and exercise, with a total of 54 book chapters and 396 papers covering a range of topics, from cell and molecular biological aspects, to mathematical modeling, integrative physiology and clinical studies.

In the 1980’s Dr. Naeije served as secretary of the working group on the Right Ventricle of the European Society of Cardiology and was Chairman of the Pulmonary Circulation group of the European Respiratory Society in the 1990’s. He has been a member of the editorial board of the American Journal of Respiratory and Critical Care Medicine, and is currently Associate Editor of the European Respiratory Journal.

Dr. Naeije has participated actively at the World Symposia on Pulmonary Hypertension in 1998 (Evian), 2003 (Venice), 1998 (Dana Point) and 2013 (Nice).

One of his major interests is high altitude adaptation and he has directed several medical research expeditions to Peru, Bolivia, Ecuador, Nepal and Kyrgyzstan and been regularly involved in studies in the Italian Alps.

They have conducted a continuous Clinical Research Center programme of phenotyping and genotyping patients with pulmonary hypertension for more than 30 years.

Dr. Newman authored the New England Journal of Medicine paper, reporting the novel insights in BMPR2 and clinical presentation from the largest known family with heritable PH. He mentors and assists in the development of multiple fellows and faculty in studies of pulmonary hypertension, leading Vanderbilt to a large comprehensive pulmonary hypertension programme spanning clinics, clinical trials and genomics and signaling studies. He is funded by NIH, together with Co-I Dr. Anna Hemmes, for studies in the metabolic syndrome through the NIH P01 and the NIH P4DIMS network.

Dr. Newman, together with John Phillips, is also Co-PI of the new Undiagnosed Disease Network at Vanderbilt, a multicenter programme to diagnose ultra-rare diseases. He is President of the CMREF; a non-profit fund that conceived and supports the Pulmonary Hypertension Breakthrough Initiative (PHBI), which is a consortium that harvests PH lungs. Recently, Dr. Newman and Dr. Rizwan Hamid found the variant in HIF2a that causes Brisket disease in cattle, a form of high altitude pulmonary hypertension.

They obtained his medical degree from Justus Liebig University Giessen, Germany in 1984, and his Research Fellow, Physiological Institute of the Medical Faculty, Justus-Liebig University in 1988. Honours and Awards: he has achieved include: Carl-Dielemann-Award for the best Doctoral Thesis, State of Hessen, Germany; Patent submission for a novel therapy for pulmonary hypertension; Patent submission for non-invasive measurement of pulmonary arterial pressure by means of MRI; Patent submission for non-invasive assessment of pulmonary hypertension by means of dynamic CT; and Patent 512393 granted and awarded with the inventeam2013 award by Austrian Patentamt. Dr. Olischenski cites among his many career related activities the design and performance of a German multicentre study with inhaled iloprost for the treatment of severe pulmonary hypertension (investigator IND); a participant in the 2nd WHO Conference on Primary Pulmonary Hypertension in Evian, France; Co-Principle Investigator (with Prof. Seeger) in a German multicentre programme to diagnose ultra-rare diseases. He is President of the CMREF; a non-profit fund that conceived and supports the Pulmonary Hypertension Breakthrough Initiative (PHBI), which is a consortium that harvests PH lungs during transplantation and coordinates scientific studies on the tissues, DNA, cells and fluids from these lungs. Recently, Dr. Newman and Dr. Rizwan Hamid found the variant in HIF2a that causes Brisket disease in cattle, a form of high altitude pulmonary hypertension.

John Newman
MD, PhD
Dr. Newman, together with Dr. James Loyd, is co-founder of the Pulmonary Circulation Center at Vanderbilt Pulmonary Circulation Center.

He obtained his medical degree from Justus Liebig University Giessen, Germany in 1984, and his Research Fellow, Physiological Institute of the Medical Faculty, Justus-Liebig University in 1988. Honours and Awards: he has achieved include: Carl-Dielemann-Award for the best Doctoral Thesis, State of Hessen, Germany; Patent submission for a novel therapy for pulmonary hypertension; Patent submission for non-invasive measurement of pulmonary arterial pressure by means of MRI; Patent submission for non-invasive assessment of pulmonary hypertension by means of dynamic CT; and Patent 512393 granted and awarded with the inventeam2013 award by Austrian Patentamt. Dr. Olischenski cites among his many career related activities the design and performance of a German multicentre study with inhaled iloprost for the treatment of severe pulmonary hypertension (investigator IND); a participant in the 2nd WHO Conference on Primary Pulmonary Hypertension in Evian, France; Co-Principle Investigator (with Prof. Seeger) in a German multicentre programme to diagnose ultra-rare diseases. He is President of the CMREF; a non-profit fund that conceived and supports the Pulmonary Hypertension Breakthrough Initiative (PHBI), which is a consortium that harvests PH lungs during transplantation and coordinates scientific studies on the tissues, DNA, cells and fluids from these lungs. Recently, Dr. Newman and Dr. Rizwan Hamid found the variant in HIF2a that causes Brisket disease in cattle, a form of high altitude pulmonary hypertension.

Herst Olischewski
MD, PhD
Dr. Olischewski is a Professor of Pulmonology and Director of the Division of Pulmonology, Department of Internal Medicine, Medical University of Graz, Austria.

He obtained his medical degree from Justus Liebig University Giessen, Germany in 1984, and his Research Fellow, Physiological Institute of the Medical Faculty, Justus-Liebig University in 1988. Honours and Awards: he has achieved include: Carl-Dielemann-Award for the best Doctoral Thesis, State of Hessen, Germany; Patent submission for a novel therapy for pulmonary hypertension; Patent submission for non-invasive measurement of pulmonary arterial pressure by means of MRI; Patent submission for non-invasive assessment of pulmonary hypertension by means of dynamic CT; and Patent 512393 granted and awarded with the inventeam2013 award by Austrian Patentamt. Dr. Olischenski cites among his many career related activities the design and performance of a German multicentre study with inhaled iloprost for the treatment of severe pulmonary hypertension (investigator IND); a participant in the 2nd WHO Conference on Primary Pulmonary Hypertension in Evian, France; Co-Principle Investigator (with Prof. Seeger) in a German multicentre programme to diagnose ultra-rare diseases. He is President of the CMREF; a non-profit fund that conceived and supports the Pulmonary Hypertension Breakthrough Initiative (PHBI), which is a consortium that harvests PH lungs during transplantation and coordinates scientific studies on the tissues, DNA, cells and fluids from these lungs. Recently, Dr. Newman and Dr. Rizwan Hamid found the variant in HIF2a that causes Brisket disease in cattle, a form of high altitude pulmonary hypertension.

Philippe Herve
Paris, ERS Task Force: Exercise hemodynamics.
Several book chapters on infectious disease.

261 articles in peer-reviewed journals and of Editor-in-Chief of Infectious Disease Reports.

Multidrug resistant organisms and by emerging infections, particularly those caused by severe, healthcare-acquired and systemic infections.

His clinical and research interests focus on the Ebola Crisis Unit.

Rome, Italy, where he is Coordinator of the Department at the national Institute for Infectious Diseases 'Lazzaro Spallanzani'.

University 'La Sapienza', Rome; Researcher at the Clinical Microbiology Institute of University of Groningen UMCG, Groningen, Zagreb, Croatia. He is also Past President of the Italian Society for Health Care Associated infections, Radiation, Urgent Care, Critical Care, and Emergency Medicine.

He is one of the world's most recognised experts on pulmonary vascular diseases. For more than three decades he has dedicated his research and clinical efforts to finding better solutions for pulmonary hypertension.

He has authored over 220 peer-reviewed articles in peer-reviewed journals, is a member of a number of medical organisations and has served as the chair of the working group on Pulmonary Hypertension of the German Cardiac Society (DGK). He is an elected Nucleus Member of the Society of Cardiology (ESC). He is also on the reviewing boards of several research organisations including the Deutsche Forschungsgemeinschaft (DFG).

He has published hundreds of clinical articles and book chapters on pulmonary hypertension and HIV. He was WHO clinical consultant in Lagos, Nigeria for the recent Ebola epidemic.

He obtained his MD degree from the Justus Liebig University of Giessen, Germany, in 1994 and subsequently completed a fellowship in cardiology at the University of Cologne. Following his doctoral thesis, he undertook a post-doctoral fellowship at Harvard Medical School, USA, before returning to Cologne.

He is currently head of the Centre for Pulmonary Hypertension at the University of Cologne, and also serves as chairman of the Cologne Cardiovascular Research Centre (CCRC). In addition he leads a basic research group that focuses on signal transduction and the biological importance of tyrosine kinases in cardiovascular disease.

Dr. Rosenkranz has published over 200 articles in peer-reviewed journals, in a number of medical organisations and has served as the chair of the working group on Pulmonary Hypertension of the German Cardiac Society (DGK). He is an elected Nucleus Member of the Society of Cardiology (ESC), and is also on the reviewing boards of several research organisations including the Deutsche Forschungsgemeinschaft (DFG).

Dr. Rosenkranz has been involved in numerous clinical trials in cardiology which, in the field of pulmonary hypertension include, AMBITION; SERAPHIN; GRIPHON; PATENT: CHEST; LEPTH; DILATE; MELODY and SUPER.

He is a Steering Committee member of the European Society of Cardiology (ESC). He has been involved in the basic and clinical investigation of pulmonary vascular diseases for nearly 40 years.

He has authored over 220 peer-reviewed publications and 74 book chapters, edited six books on the pulmonary circulation and has served as Principal Investigator/Steering Committee Chair or Member for pivotal trials of most of the currently approved medical therapies for PAH. He has received numerous honours and awards, including an Honorary Fellowship by the Royal College of Physicians, United Kingdom, the Dickinson Richards Award from the American Heart Association, and the Simon Ark Award from the American College of Cardiology.
Julio Sandoval MD
Julio Sandoval is Professor of the Postgraduate Course on Cardiopulmonary Medicine of the National University of Mexico.

He was Head of the Cardiopulmonary Department of the National Institute of Cardiology in Mexico until 2011 and is currently Deputy Director of Clinical Research at the same institution. He is a member of the National Academy of Medicine and of the National System of Investigators in Mexico. Professor Sandoval is founder and ex-Chairman of the Pulmonary Circulation Assemblies of the Latin American Society of Thorax (ALAT), a branch of the American Thoracic Society, and of the Mexican Society of Cardiology. He has been member of the Scientific Leadership Council of the Pulmonary Hypertension Association and he is a founder fellow of the Pulmonary Vascular Research Institute (PVRI).

He has been an invited lecturer at several international meetings of the American College of Cardiology, European Society of Cardiology, American Thoracic Society, World Heart Federation, and PVRI. Professor Sandoval has also been an active member of the international task forces for the Scientific Federation, and PVRI India Task Force.

BKS Sastry
Dr. Sastry obtained his internal medicine and cardiology training at PGIMER, Chandigarh, India and graduated in 1990.

He is currently working as Consultant Cardiologist in CARE hospitals, Hyderabad, India where he has been since 1997. He specializes in clinical cardiology with a special interest in clinical research and has carried out a small, single centre randomised controlled clinical trial of sildenafil in PAH before the SUPER trial was published. Subsequently, he participated as investigator in STARS 1 and 2, SERAPHINE, GRIPHON and other clinical trials in PAH. There is no formal PAH clinic at his centre but he personally looks after the majority of PAH patients at his hospital.

Along with the Genetics Department of Osmania University he is involved with genetic studies in PAH but not any frontier research. Dr. Sastry’s main area of clinical specialization is general cardiology including interventional cardiology. PAH practice forms about 5 to 10 per cent of his overall practice. For the last year, he has been president of PVRI India Task Force.

Ralph Schermuly MD PhD
Ralph Schermuly is an expert in the field of experimental pathophysiology and pulmonary hypertension, and has been Professor for Pulmonary Pharmacotherapy at Justus Liebig University Giessen, Germany, since 2011.

Dr. Schermuly is the co-author of more than 200 peer-reviewed publications and is currently Principal Investigator on a number of grants from the German Research Foundation ‘Deutsche Forschungsgemeinschaft’ (DFG). He is a member of the German Lung Center (DZL), the steering committee of the Excellence Cluster Cardio-Pulmonary System (ECCPS) and the Universities of Giessen and Marburg Lung Center (UGMLC).

Examples of his ‘from bench to bedside’ research include preclinical investigations of inhaled prostansoids, phosphodiesterase inhibitors, stimulators of soluble guanylate cyclase, receptor tyrosine kinases and transbronchial surfactant application. Thus providing the basis for worldwide approval of inhaled iloprost, oral sildenafil and riociguat for the treatment of pulmonary arterial hypertension.

Werner Seeger
Professor Seeger is based at the Department of Internal Medicine, Justus Liebig University, Giessen, where he is the Medical Executive Director of the University Hospital, Giessen and Marburg.

His main areas of research include pulmonary circulation, acute lung injury, pneumonia and sepsis, chronic respiratory failure and aerosol medicine.

He is Advisory Editor, and part of the Editorial Board, for the American Journal of Physiology and the American Journal of Respiratory and Critical Care Medicine.

He has held numerous academic posts and is currently Chair of the German Centre for Lung Research (DZL): Chairman of the ‘Universities of Giessen and Marburg Lung Centre’, Spokesman of the German Department Chairs of Internal Medicine: Director of the ‘Lung Development and Remodeling’, Chair at the Max Planck Heart and Lung Institute, W.G. Kerpff Institute, Bad Nauheim; Coordinator of the Excellence Cluster ‘CardioPulmonary System’, Managing Director, Department of Internal Medicine, JLU School of Medicine, and Chair, TransMIT GmbH, Medical Technology.

Over the course of his career he has also received several awards/honours. In 2000 he was elected to the German Academy of Natural Sciences Leopoldina and in 2008 received the Robert-Pfleger Award. Most recently, in 2014, he gave the AHA Dicksonson W. Richards Memorial Lecture. He was awarded the Von Behring Röntgen Research Medal and was the ERS Congress Chair Awardee.

Onno Anthonius Spruijt
Onno Anthonius Spruijt graduated in 2011 from the Medical School at the University of Amsterdam (AMC).

After working as a resident in the Department of Internal Medicine, St. Antonius Hospital, Utrecht, he started, in 2012, to work as an investigator in the field of pulmonary hypertension at the department of Pulmonary Medicine, VU University Medical Center in Amsterdam under the supervision of Harm-Jan Bogaard and Anton Vonk Noordegraaf.

He hopes to finish his thesis next year and start his specialisation in Pulmonary Medicine in the summer 2016.
Kurt R. Stenmark
Dr. Stenmark is Professor of Paediatrics, Head of the Division of Paediatric Critical Care Medicine and Director of the Cardiovascular Research Laboratory at the University of Colorado Denver (UCD) and The Children’s Hospital Colorado in Aurora, Colorado.

He joined the paediatric faculty at UCD in 1984 as an Assistant Professor, was made Associate Professor with Tenure in 1989 and full Professor with Tenure in 1994. He has been the Division Head of Paediatric Critical Care Medicine since 1987. Co-author of over 275 publications, Dr. Stenmark is currently Principal Investigator on a number of NIH grants (including a PPG, ROI A1s, and a T-32 Training Grant) in the areas of immature pulmonary circulation, hypoxic vascular modeling, and pediatric pulmonary disease. Additionally, he provides research support on a number of other NIH grants. Since 1984, the NIH has continuously funded him. He has received numerous international honors and awards, sits on several national and international committees as well as major grant review committees in his field (permanent member of RIBT and NHLBI). He is an Affiliate Faculty for the Center for Global Public Health. Dr. Stenmark has been a visiting professor or invited speaker throughout Europe and North America.

Dr. Stenmark has served in the capacity of both Chair of the Pulmonary Circulation Nominating Committee and Chair of the Pulmonary Circulation Section of the ATS. He has served on the planning committee for several international vascular biology meetings, for the ATS sponsored Grover Conference on the Pulmonary Circulation in Beijing, China. Most recently, he was appointed to the Pulmonary Vascular Research Institute (PVRI) Steering and Scientific Committee. Dr. Stenmark is the honored recipient of the 2015 Robert F. Grover Prize from the American Thoracic Society.

Kent L. Thornburg, MD
Kent L. Thornburg serves as the Lowell Edwards Chair of Cardiovascular Research, Professor of Medicine in the Knight Cardiovascular Institute at the Oregon Health & Science University and holds joint professorships in the Departments of Physiology & Pharmacology, Biomedical Engineering and Obstetrics & Gynecology.

He serves as director of the Center for Developmental Health in the Knight Cardiovascular Institute and director of the OHSU Bob and Charlee Moore Institute for Nutrition & Wellness. He has expertise in cardiopulmonary physiology, placentology, and developmental programming. Kent Thornburg studies the physiological adaptations to pregnancy and the roles of maternal diet and body composition in regulating placental and fetal growth and lifelong health. He collaborates with scientists in England, New Zealand, Switzerland, Finland and Australia and oversees clinical studies in rural Oregon and Alaska.

He served as editor of the international journal, Placenta, and as consulting editor for Pediatric Research. He currently sits on the editorial board of the American Journal of Physiology. Kent Thornburg serves regularly on advisory panels at the National Institutes of Health, the American Heart Association and the Children’s Heart Foundation and serves on the medical advisory board of the Preeclampsia Foundation. Recently, he served as co-chair of the task force to determine the 10 year vision of the developmental origins of health and disease for the National Institute of Child Health and Human Development.

Mark Toshner
Dr. Mark Toshner is a chest physician at Papworth Hospital - the UK referral centre for pulmonary endarterectomy specialising in pulmonary vascular disorders. He holds an honorary contract at the University of Cambridge.

Prior to taking up his consultant post Dr. Toshner held a NIHR/Wellcome Clinical Lecturer’s post in Translational Medicine at the University of Cambridge, and a fellowship with the British Heart Foundation. He ended up in pulmonary vascular research after an accidental interest in high-altitude pulmonary physiology that has stalled recently due to the physical demands of being a lily-livered, barely-fit man entering middle age.

At some point in the future he still intends to get to the top of a mountain again, possibly with assistance.

Dr. Toshner held a NIHR/Wellcome Clinical Lecturer’s post in Translational Medicine at the University of Cambridge, and a fellowship with the British Heart Foundation. He ended up in pulmonary vascular research after an accidental interest in high-altitude pulmonary physiology that has stalled recently due to the physical demands of being a lily-livered, barely-fit man entering middle age.

At some point in the future he still intends to get to the top of a mountain again, possibly with assistance.

Carmine Darío Vizza, MD
Carmine Dario Vizza is Associate Professor of Cardiology at the Department of Cardiovascular and Respiratory Disease and Director of the Pulmonary Hypertension Clinic at the University of Rome La Sapienza, Rome, Italy.

Since 2013 he has been a member of the national board of the Italian Society of Cardiology and is the founder and president of the Italian Pulmonary Hypertension Network (IPHNET) that includes 23 Italian PH centres.

Professor Vizza has published widely in the field of pulmonary vascular physiology, pulmonary transplantation and pulmonary hypertension. He has participated as principal investigator in several international multi-centre randomised studies on pulmonary hypertension including ALPHABET, PHAST, EARLY, PHIRST, COMPASS-1, SERAPHIN, AMBITION.

He served as a member of the committee of the COMPERA registry. His interests have focussed on developing a translational center that integrates clinical and basic research and focuses on a better understanding of the pathogenesis of pulmonary vascular remodeling and the physiology of right ventricular adaptation to changes in the pulmonary vascular bed.

Dr. Waxman’s academic focus includes the role of inflammatory mediators in pulmonary vascular remodeling and right ventricular-pulmonary arterial coupling.
Health Research.

Wellcome Trust and the National Institute of Foundation, Medical Research Council, the role of iron homeostasis and zinc biomarkers. More recently he has investigated signalling pathway and circulating drug targets and better ways of monitoring hypertension with a view to identifying novel biomarkers.

He has published widely on the cyclic GMP disease.

He has spent the past 25 years investigating the molecular pathology of pulmonary hypertension with a view to identifying novel drug targets and better ways of monitoring the disease.

He has published widely on the cyclic GMP signalling pathway and circulating biomarkers. More recently he has investigated the role of iron homeostasis and zinc transport in pulmonary vascular disease.

His research is supported by the British Heart Foundation, Medical Research Council, the Welcome Trust and the National Institute of Health Research.

His interest in pulmonary vascular biology began with his PhD, published in 2002, demonstrating an autocrine role for endogenously released endothelin-1 in the proliferation of human pulmonary artery smooth muscle. After finishing clinical training in respiratory medicine, general medicine and intensive care medicine, he was appointed consultant in pulmonary hypertension and intensive care medicine at the Royal Brompton Hospital (RBH), in London. In 2007 he was awarded a prestigious, “new blood”, clinical senior lectureship at Imperial College. He has been Clinical Lead for the National Pulmonary Hypertension service at RBH since 2009 and is currently Chair of the Pulmonary Vascular Disease Specialist Advisory Group for the British Thoracic Society and a member of the NHS England, Pulmonary Hypertension Clinical Reference Group.

He has maintained his research interest and published over 70 papers; current interests include the role of inflammation in the pathogenesis of pulmonary vascular remodelling, skeletal muscle dysfunction associated with pulmonary arterial hypertension and pulmonary hypertension associated with chronic respiratory diseases.

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He is also Professor of Cardiothoracic Surgery at the National Heart and Lung Institute, Imperial College London and Founder and Director of Research at Harefield Heart Science Centre (Magdi Yacoub Institute) overseeing 60 scientists and students focused on tissue engineering, myocardial regeneration, stem cell biology, end stage heart failure and transplant immunology.

Professor Yacoub established the largest heart and lung transplantation programme in the world where more than 2,500 transplant operations have been performed. He has also developed novel operations for a number of complex congenital heart anomalies as well as leading research including tissue engineering heart valves, myocardial regeneration, novel left ventricular assist devices and wireless sensors with collaborations within Imperial College, nationally and internationally.

Sir Magdi has an active interest in global healthcare delivery with focus on developing programmes in Egypt, The Gulf Region, Mozambique, Ethiopia and Jamaica.

He is Founder and President of the Chain of Hope charity, treating children with correctable cardiac conditions from developing countries and establishing training and research programmes in local cardiac units.

Dr. Yuan received his medical training at Suzhou Medical College (China), his PhD at Peking Union Medical College (China) and his postdoctoral training at the University of Maryland School of Medicine. His pulmonary vascular disease research leads the field on pathogenic roles of membrane receptors and ion channels and provides a new research direction for developing therapeutic approaches for the disease. Dr. Yuan is a fellow of the American Heart Association, the American Association for the Advancement of Science, and the American Physiological Society. He is also an elected Member of the American Society for Clinical Investigation and the Association of American Physicians, and was a Guggenheim fellow.

Dr. Yuan has served on many advisory committees and editorial boards, including Chair of the Respiratory Integrative Biology and Translational Research study section of the National Institutes of Health (NIH), and Chair of the Pulmonary Circulation Assembly of the American Thoracic Society.

He is currently a regular member of the Vascular Cell and Molecular Biology study section of the NIH, Editor-in-Chief of the Journal of Pulmonary Circulation, and Deputy Editor and Associate Editor of the American Journal of Physiology-Cell Physiology.

Sir Magdi Yacoub
FRS
Sir Magdi Yacoub is Executive Director of Qatar Cardiovascular Research Center and Hamad Medical Corporation.

Jason K-J Yuan
MD, PhD, FAHA
Dr. Jason Yuan is Professor of Medicine and Associate Vice President for Translational Health Sciences at the University of Arizona in Tucson, AZ. He is also Head of the Division of Translational and Regenerative Medicine in the Department of Medicine at the University of Arizona College of Medicine.

He is also Professor of Cardiothoracic Surgery at the National Heart and Lung Institute, Imperial College London and Founder and Director of Research at Harefield Heart Science Centre (Magdi Yacoub Institute) overseeing 60 scientists and students focused on tissue engineering, myocardial regeneration, stem cell biology, end stage heart failure and transplant immunology.

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Employing innovative experimental approaches, she leads a research programme directed at identifying novel drug targets for pulmonary hypertension and developing biomarkers for assessing response to therapy.

Dr. Zhao is recognised for establishing the importance of the cGMP signalling pathway in pulmonary vascular homeostasis which contributed to the identification of phosphodiesterase type 5 (PDE5) as a key therapeutic target for pulmonary hypertension, as well as her recent work on HDAC inhibitors and iron supplementation.

Most recently, her research has led to a groundbreaking observation that zinc transporter, ZIP12, has a fundamental role in mammalian pulmonary vascular homeostasis and offers a new drug target for pulmonary hypertension (Nature 2015). To overcome the challenge of evaluating interventions for pulmonary hypertension on the pathology of the disease, she has applied cutting edge PET imaging methodology, establishing this as an effective tool for disease assessment with enormous potential for stratified medicine.

Lan Zhao
MD, PhD, FAHA
Dr. Lan Zhao is Senior Lecturer of Experimental Medicine at Imperial College London and Academic Director of the Imperial College Preclinical Biological Imaging Centre.

Our Speakers, Chairs & Commentators LISTED IN ALPHABETICAL ORDER
Dr. Zhenguo Zhai is board certified in Pulmonary and Critical Care medicine. He was educated at Qingdao Medical College and Capital Medical University, received his training in internal medicine at the Affiliated Hospital of Qingdao Medical University and completed his training in pulmonary and critical care medicine at Beijing Institute Respiratory Medicine, Beijing Chaoyang Hospital. He adapted his MRes of translational medicine at Imperial College London. Currently, he is Associate Professor and Chief Physician in the Department of Pulmonary and Critical Care Medicine, China-Japan Friendship Hospital. Dr. Zhai serves as the Secretary and Vice-director of Assembly of Pulmonary Embolism and Pulmonary Vascular Diseases in the Chinese Thoracic Society. He also serves as a fellow of Pulmonary Vascular Research Institute (PVR) and is a member of the American College of Chest Physicians (ACCP).

Dr. Zhai is the author of numerous articles and chapters and is a contributor to teaching of acute venous thromboembolic disease and pulmonary hypertension. In his research, he has actively participated in clinical and translational studies about genetic polymorphisms; studies of pulmonary embolism, inherited mechanisms of the development of pulmonary embolism and chronic thromboembolic pulmonary hypertension; cardiopulmonary function and biomarker response of pulmonary hypertension and chronic thromboembolic pulmonary hypertension; and randomized clinical trials of thrombolytic and anticoagulant therapy of thromboembolic diseases. Other current research interests are in management of venous thromboembolism, acute and longer-term management of pulmonary embolism and pulmonary hypertension. He is clinically active as a teaching physician staffing fellows, residents, and medical students at Capital Medical University and Peking University.

“Research makes everything possible.”
Please join us at the **Gala Dinner on Saturday 16th January 2016** which will be held at the Ristorante L’Archeologia.

To reserve your place, please visit the PVRI registration desk during the Congress. As in previous years, we ask for a small charge of €25. We will meet at 7pm promptly in the hotel reception where transport to and from the restaurant will be available.

As is tradition, during the Gala Dinner, we will present the three **PVRI 2015 Awards** - the Lifetime Achievement Award, the Achievement Award and the Certificate of Excellence. We will also announce the most active members of the PVRI Committee for Young Clinicians & Scientists who have achieved the highest points during 2015.

The evening will give you a ‘taste of Italy’ accompanied by local musical entertainment in a relaxed and festive atmosphere.
“During time away from the Congress, have a wish at the Trevi Fountain and sample some classic Italian cuisine and Roman culture.”

CME credits
This event has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME) and is designated for a maximum of, or up to 17 European CME credits (ECMEC).

Timetable of Events...
Welcome

Advances in our understanding of Pulmonary Vascular Disease
Chairs and Facilitators: Stuart Rich, C. Dario Vizza, Kurt Stenmark
The early life roots of chronic disease // Kent Thornburg
Genetic pre-disposition to develop PVD // Nick Morrell
The metabolic basis of PAH // Evangelos Michelakis
Systems biology in PAH: an integrated approach to a complex disease // Brad Maron
Discussion

Coffee

Current Approaches to Diagnosis and Management
Chairs and Facilitators: Sean Gaine, Stephen Archer and Stefano Ghio
Current Guidelines: Can we do better? Are we moving in the right direction? // Lewis Rubin
Ensuring best quality of care in developing countries // Majdy Idrees
Heart sound analysis in the diagnosis of pulmonary hypertension // Ian Adatia
Discussion

Lunch

Using functional capacity or reserve to evaluate PAH Patients
Chairs and Facilitators: Maria del Cerro, Ioana Preston
Assessing the functional reserve of the right ventricle // Stefano Ghio
Assessing functional capacity in adults // Robert Naejie
Assessing functional capacity in children // Astrid Lammers
Discussion

New approaches to studying PVD
Chairs and Facilitators: Kurt Stenmark, Werner Seeger
Human lung-on-a-chip models // Donald Ingber
What do the rat, mouse, pig and human have in common? // Ralph Schermuly
Discussion

Tea

Moderated Poster Sessions: Meet the Experts addressing the topics discussed at today's sessions

PVRI Annual General Meeting
Welcome Reception
Itinerary // Programme

Wednesday 13th January

10.00am - 17.00pm
PVRI Council Meeting // Colosseum Room
Led by Sheila Glennis Haworth

PVRI Pre-Clinical and Molecular Task Force //
San Pietro Room
Led by Mandy Maclean

13.00pm - 17.00pm
PVRI Paediatric Task Force // Terrazza Monte
Mario Room
Led by Ian Adatia

Thursday 14th January

08.45am - 17.15pm
1st Day of PVRI Annual World Congress on PVD
1st Day of Scientific Agenda

17.30pm - 18.30pm
PVRI Annual General Meeting

18.30pm - 20.00pm
Cocktail Networking Reception

20.00pm - 22.00pm
PVRI Imaging Task Force // Corner Suite Room
Led by David Kiely

PVRI CYCS Meeting // Salone dei Cavelieri
Room
Led by Djuro Kosanovic
### New frontiers in imaging the pulmonary hypertensive patient
Chairs and Facilitators: Evangelos Michelakis, Krishna Kumar

- The role of imaging in the PH clinic // David Kiely
- Nuclear medicine and CT imaging in PH // Horst Olschewski
- Repeated assessment of RV structure and function during follow-up with MRI // Onno Spruijt

#### Discussion

Biology of lung and cardiac stiffening // Kurt Stenmark

- Imaging and inflammation in PAH: 18FDG Positron Emission Tomography // Lan Zhao

#### Discussion

Coffee

### Echocardiography

- Echocardiography for differentiating pre-capillary from post-capillary PH: Tool or toy? // Michele D’Alto

#### Discussion

### Preventing the Eisenmenger Syndrome
Chairs and Facilitators: Magdi Yacoub, Sheila G. Haworth

- A public health perspective // Krishna Kumar
- Experience in Brazil // Maria Angelica Binotto
- Experience in Bolivia // Alexandra Heath

#### Discussion

### Moderated Poster Sessions & Meet the Experts

Lunch
Itinerary // Programme

Friday 15th January

08.30am - 13.00pm

2nd Day of the Scientific Agenda

13.00pm

Sight-seeing tours.
For more information, please visit the PVRI Reception Desk

13.30pm - 17.00pm

EU Paediatric Network // Salone dei Cavalieri Room
(Booked till 6.00pm)
Led by Georg Hansmann

PVRI Right Heart Failure & Exercise Task Force
// Tevere Room
Led by David Systrom

PVRI Women’s Pregnancy Task Force // Corner Suite Room
Led by Anna Hemnes
### Scientific Agenda // Programme Saturday 16 January

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<td><strong>Current therapies: How the drugs work and their optimal usage.</strong></td>
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<td>Will they work in my patient?</td>
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<td>Chairs and Facilitators: Stuart Rich, Joan-Albert Barbera</td>
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<td><strong>Overview of current therapies</strong></td>
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<td><strong>How we think the drugs may work: sex differences</strong></td>
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<td><strong>Current use of combination therapy</strong></td>
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<td><strong>Predicting therapeutic response: pharmacogenetics in PVD</strong></td>
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<td>Chairs and Facilitators: Julio Sandoval, Shahin Moledina</td>
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<td><strong>Prescribing with limited financial resources</strong></td>
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<td><strong>A novel therapeutic approach: Potts Shunt</strong></td>
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<td><strong>Advancing our approach to medical therapy</strong></td>
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<td>Chairs and Facilitators: John Newman, Pilar Escribano-Subias</td>
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<td><strong>New clinical trial designs for PH</strong></td>
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<td><strong>New targets, new therapies: The probable and the possible</strong></td>
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<td>Chairs and Facilitators: John Newman, Jason Yuan</td>
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<td><strong>Immune targets</strong></td>
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<td><strong>Mediators of inflammation in congenital heart disease associated with PH</strong></td>
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<td>// Antonio Lopez</td>
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<td><strong>HIV:</strong></td>
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<td>Potential interaction between antiretroviral drugs and PH specific therapies</td>
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<td><strong>Antibodies as therapy in PVD?</strong></td>
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<td>// Allan Lawrie &amp; Nick Morrell</td>
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<td><strong>Targeting metabolic change</strong></td>
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<td>// Stephen Archer</td>
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<td><strong>Hot topic: the metal story and PH</strong></td>
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Itinerary // Programme

Saturday 16th January

09.00am - 16.15pm
3rd Day of Scientific Agenda

07.00am - 22.00pm
Gala Dinner & PVRI Achievements Awards
Ceremony at Ristorante L’Archeologia
## Scientific Agenda // Programme Sunday 17 January

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<td><strong>Emerging clinical challenges for the PH specialist</strong>&lt;br&gt;Chairs and Facilitators: Dario Vizza, Lewis Rubin, Maria Angelica Binotto</td>
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<td>Heart failure with preserved ejection fraction: diagnostic challenges // Stephan Rosenkranz</td>
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<td>Heart failure with preserved ejection fraction: therapeutic challenges // Marco Guazzi</td>
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<td>Phenotypic differences in RV remodeling // Paul Hassoun</td>
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<td>Lung disease and PH: definitions and therapy // Werner Seeger</td>
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**PVRI Symposium: Chronic Thromboembolic Pulmonary Hypertension**<br>Chairs and Facilitators: Paul Corris, Ioana Preston

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<td>Novel concepts in aetiology of CTEPH // Mark Toshner</td>
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<td>How to approach the diagnosis of CTEPH // Zhenguo Zhai</td>
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<td>How to treat CTEPH 1 surgery // Andrea D’Armini</td>
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<td>How to treat CTEPH 2 new approaches // Paul Corris</td>
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**Closing remarks**
Held in // Salone dei Cavelieri

11.00
12.00
13.00
14.00

Sunday 17th January

08.30am - 13.30pm

Last Day of Scientific Agenda

Itinerary // Programme

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PVRI Central Asia Task Force
Ghazwan Butrous and Talant Sooronbaev

In Autumn 2014, Ghazwan Butrous visited the Institute of Cardiology and gave two talks on PVD to the staff (attended by about 50 people) and discussed PVRI and PVD issues with the centre head Prof. Berkinbaev and other invasive cardiology staff, notably Dr. Algerim Yeshtay, Head of the Dept. of Interventional Cardiology and recently appointed to run a pulmonary hypertension clinic.

PVRI Excellence Centre for Pulmonary Hypertension

We have discussed and made a decision that a PVRI excellence centre for Pulmonary Vascular Disease (based in the National Centre Cardiology and Internal Medicine (NCCIM) should be created. The Kyrgyz Republic Ministry of Health and the head of the NCCIM, Prof. Dzhumagulova, have promised to allocate the newly refurbished wing of the NCCIM. Their new PVRI excellence centre for Pulmonary Vascular Disease in Bishkek was officially opened in January 2015. This centre is now the pilot project for the CA PVRI Task Force - now called CAPH (Central Asia Pulmonary Hypertension Group).

They are keen to make the institute the PVRI Centre of Excellence for PVD in Almaty. Other centres will be in Astana (the new capital) with almost 700,000 inhabitants and growing. Ghazwan Butrous visited between 29 September - 1 October 2015 and agreed it should be another PVRI centre of excellence. Doctors and technicians have good experience, although they could benefit from more targeted training. The centre is mainly used for congenital heart diseases and left heart catheterisation. Ghazwan Butrous also visited the Institute of Paediatric Surgery and had a lengthy discussion with Dr. Abzaliev Kuat who is involved in the iloprost study to assess reversibility of pulmonary hypertension in congenital heart disease, a protocol they share with a centre in South Korea.

The centre is heavily involved in the correction of congenital heart diseases with the majority of patients of an older age group (>9 years old). Many of these patients are still suffering from high pulmonary pressure despite correction. The Cath Lab is well equipped and sufficient for the purpose and they also have two well equipped cardiac surgery theatres.

From Almaty Ghazwan Butrous travelled to Bishkek, to assess the possibility of establishing the Excellence Centre at the National Centre Cardiology and Internal Medicine (NCCIM). There they have reasonable echocardiography supported by six ultrasound doctors and scientists, some with more than 15 years’ experience. The cardiac catheterisation lab is reasonably well equipped and carries out mainly work on congenital heart disease and left heart catheterisation. However, drug availability is limited to generic sildenafil.

The facility has four rooms (one is an Echo lab), the centre will support the high altitude research which is the main research activity in Kyrgyzstan. Dr. Talant Sooronbaev and Dr. Batyr Osmonov will be running the centre.
The CAPH Excellence Centre in Bishkek main function:
1. Appoint trained doctors (main staff) to the PVRI/CAPH Excellence Centre for Pulmonary Vascular Disease and manage their main responsibilities and activities.
2. Create a team of consultants from the following disciplines: infectious diseases, rheumatology, cardiology, paediatrics, cardiac surgeons, pulmonologists, CT specialists and others to work within the Centre.
3. Provide the necessary equipment for the management of Pulmonary Vascular Disease (ECG, spirometry, Echocardiography, DLCO and others).
4. Organise a right heart catheterisation in the department of interventional cardiology of NCCIM.
5. Create and organise a PVRI EC PVD outpatient room for examination of out patients with Pulmonary Vascular Disease. Allocate four beds in the hospital for patients with Pulmonary Vascular Disease.
6. Develop a referral system for patients with Pulmonary Vascular Disease from other centres and clinics.
7. Create a database (register) of patients in the PVRI Excellence Centre for Pulmonary Vascular Disease; develop a simple programme to register all patients seen in the Centre. The main function of this database is to assess the efficiency of the centre and the referral pattern and to identify issues that can direct further training and awareness programme.
8. Professor Butrous and Dr. Majdy Idrees to be consultant and advisor of the PVRI excellence centre for Pulmonary Vascular Disease in Kyrgyzstan.
10. Organise and hold educational and awareness programmes for PH in all regions of Kyrgyzstan, involving many other disciplines and specialties.
11. Produce brochures for patients and the public on pulmonary hypertension.
12. Establish an organisation for patients with PH in Kyrgyzstan.
13. The Saudi Association Of Pulmonary Hypertension (SAPH) can support this new initiative, in both an advisory and training capacity.

PVRI Excellence Centre for Pulmonary Hypertension at SCP & PS in Almaty.
The second PVRI excellent Centre was established at The Scientific Centre of Paediatrics and Paediatric Surgery (SCP&PS) in Almaty Kazakhstan. The SCP&PS was founded in 1932 and included various for specialties for Paediatric Cardiology, Cardiac Surgery, Oncology, Haematology, Pulmonology, Rheumatology, Neonatology, and Urology. The PVRI Excellent Centre for Pulmonary Hypertension SCP&PS was established in July 2015 by Dr. Algerim Kuat and approved by the Professor Boranbayeva Director of Scientific Centre of Paediatric Surgery. The funding for SCP&PS is covered by the central budget of the Ministry of development.

The centre will:
1. Become a centre for further medical education in the field of Pulmonary Vascular Diseases by organising seminars, training programmes and masterclasses at local and regional levels.
2. Enhance scientific communications with other medical organisations in the region to exchange experience and expertise.
3. Organise a Paediatric Pulmonary Hypertension awareness day for local physicians in Kazakhstan.
4. Establish a patient data collecting system to assess the pattern and distribution of Pulmonary Vascular Diseases in Kazakhstan to help future clinical and policy strategies of the paediatric population.
5. Establish a specialist referral clinic to deal with pulmonary hypertension and its complication and advance therapies.
6. Support graduate and postgraduate students and doctors in training to pursue further research in Pulmonary Vascular Disease.
7. Enhance clinical research collaboration with international centres of excellence.
8. Work with the PVRI paediatric and congenital heart disease task force and support its activities.

PVRI Trainings and Masterclasses
Two masterclasses took place in: Bishkek, Kyrgyzstan 23-25 April organised by Dr. Sooronbaev, and Astana, Kazakhstan 1-2 October 2015 organised by Dr. Murat Mukarov.

Participants at the master class in Bishkek.

The general structure of the two masterclasses:
1. One day general training course (mainly in Russian) on pulmonary vascular diseases. Main participants were local consultants with lectures from guest speakers Ghazwan Butrous, Stefano Ghio and Tarek Kashour.
2. This was followed by a full day of two separate groups:
   a. Echocardiography with participation by a panel of experts (lead by Dr. S. Ghio from Italy), which involved theory and live demonstration of clinical cases.
   b. Right heart catherization with participation by a panel of experts (lead Dr. T. Kashour from Saudi Arabia), which involved theory and live demonstration of clinical cases.

CAPH Young Group
Professor Butrous met a group of young physicians interested in pursuing careers in pulmonary hypertension and in further research.

Professor Ghazwan Butrous holds a master class.

This will form part of the CAPH and PVRI CYCS. The current organisers of the Young Group are Dr. Abzaliev Kuat and Dr. Batyr Osmonov. Dr. Kuat has established a special Facebook page for CAPH Young Group and contributed to an article (in Russian) in the current issue of PVRI Chronicle.
THE PATHWAY TO BREAKTHROUGH THERAPIES.
This year the Annual Congress of the European Respiratory Society (ERS) took place in Amsterdam from 26-30th September 2015 (Figure 2). The “city of bicycles” is the capital of Netherlands, and known for many things, for instance their abundance of canals (“Grachten”), museums, coffee shops, cheese and the Red Light District (Figure 4).

More than 22,000 people from more than 127 countries, scientists and clinicians, attended this meeting reaching the highest number of attendees ever. Increasing number of attendees documents the increasing interest in pulmonary diseases as the major causes of death worldwide. The need to develop new drugs caused more investments in the respective scientific field in the recent past. The “harvest” of these investments is a variety of qualified people with an abundance of possibilities, both from the technical as well as infrastructural point of view, resulting in important advances in the field.

As usual, the ERS congress was a nice platform for scientists from all over the world to meet, present and discuss their data and news about lung diseases. New findings concerning mechanisms and possible future treatments of pulmonary diseases were presented as talks and posters.

In particular, e-cigarettes were a hot topic. More and more people recognize that these “alternatives” to conventional cigarettes may have harmful effects as well and that they may not really help for smoking cessation. This topic is also presented in Interactive Discussion part of this issue of the PVRI Chronicle. In brief, some animal studies showed that e-cigarettes containing nicotine cause similar acute inflammatory response to conventional cigarettes. However, long-term effects of these electronic cigarettes are still unknown and under investigation. Interestingly, a retrospective view at available data led to the conclusion that in most cases e-cigarettes do not help quitting smoking but just lead to a shift from conventional to e-cigarettes. Moreover, let’s quote here insightful comment from an audience which was in turn: “Originally, e-cigarettes were developed and introduced by the tobacco smoke industry, an industry which spent a lot of effort to make users addicted to cigarettes. Do you really believe that the same industry now wants their customers to get rid of smoking?”. Having this in mind, the outcome of studies investigating the safety and benefit of e-cigarettes in comparison to conventional ones will be of interest.

Similar to last year in Munich, just few members of the CYCS attended the ERS. Nevertheless, we (Michael Seimetz, Mario Boehm, Balram Neupane, Michiel A. de Raaf) met and discussed current issues related to the CYCS committee (Figure 5). Amongst others, we were talking about our annual point system and the travel grants provided for extraordinary activity of our members. Although without final decision, we were thinking about quantity and grant amount as well as maybe to provide official certificates which emphasize the tribute for the efforts spent for the PVRI.
facilitated to get in contact with other young scientists. Young people had the opportunity to meet and interact with respiratory medicine and ERS leaders. Many people attended and many quite active discussions followed with strangers, who swiftly became friends and potential collaboration partners.

At this point, it is worth to mention that one of our most active CYCS members and at the same time the secretary of our CYCS committee, Michiel Alexander de Raaf, got awarded with the ERS PAH Fellowship (figure 6). On behalf of all CYCS members we would like to congratulate to our friend for this extraordinary achievement. Moreover, Michiel is a very good example that our ambitious committee consists of high quality scientists with great potential which can help to develop the CYCS becoming one of the most important committees of the PVRI in future.

Apart from our own PVRI annual congress, the ERS is a good opportunity for our committee to meet and discuss issues concerning the PVRI and the CYCS vis-à-vis. Thus, we encourage more young PVRI members to participate in this congress in future so that more interesting, interactive and fruitful discussions can take place along with brainstorming of new ideas.

Finally, Amsterdam with its Venice-like character is a recommendable place for congresses and scientific discussions.

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Figure 4: The beautiful sights of Amsterdam, as pictured by Michael Seimetz
Figure 2:
European Respiratory Society (ERS) congress in Amsterdam, Netherlands

Figure 3:
Amsterdam/Netherlands, famous for bicycles and cheese

Figure 6:
Appreciation of our colleague Michiel Alexander de Raaf receiving the ERS PAH Fellowship. Congratulations!
Team PHenomenal Hope – Racing to make a difference in the lives of PH patients

Patricia George

This past year has been exciting for Team PHenomenal Hope, non-profit endurance team that races with the Pulmonary Hypertension community. In 2015 we expanded our team from a team of four, focusing on one event, to a team of 14, putting ultra-cyclists, runners, swimmers and triathletes into races all over the country and world. Our athletes represented the PH community in events all over the map, on three continents, in the belief that big sporting events can serve as a lightning rod to raise awareness about pulmonary hypertension.

Getting started in 2016 with new epic events In 2016 our team looks forward to new events, new opportunities to stretch our limits, and new team members to help make it happen. And it will get off to an early start as our first major race brings Hap Farber onto our team, racing with Patricia George as a PH physician duo, in The Pioneer New Zealand, a mountain bike stage race over the Southern Alps. They will be joined by Kristen Engle and Thea Kent, and the four will race 546 km with over 15,000 meters of climbing in 7 days. This event will also kick off our organization’s #LiveYourDream campaign, connecting endurance athletes with the PH community, in the shared goal of going after that “epic” in each of our lives. Later in the year you’ll be seeing more from team members as we continue to do new and exciting endurance events all over the globe.

Our most exciting news yet: Introducing Team PHenomenal Hope Brazil! Inspired by Team PHenomenal Hope’s success in the Race Across America in 2014, Paula Menezes, president of the Brazilian Pulmonary Hypertension Association, has formed a 4-person ultra-running team, who will race in 2015 to raise awareness about pulmonary hypertension and strive to make more PH therapies available to PH patients in Brazil. The team will be building toward the big race in October, when they join with runners from Team PH USA to race the Bertioga Maresias, a 75 km race, for PH patients in Brazil and around the world. For more information, check out their website at: http://teamphenomenalhope.org.br

Call to Action:

We invite the PVRI community to race with us in this PH race. Are you racing in an event near you and want to help us put PH even more on the map? Race with us as a Team PH Ambassador! No time to race, but want to support our cause, please make a secure, tax-deductible donation to our cause at teamphenomenalhope.org.

To find out more about Team PHenomenal Hope, please check out our website, like us on Facebook, and follow us on Twitter and Instagram.

Corresponding Author

Patricia George, MD
Assistant Professor of Medicine, UPMC, Pittsburgh, Pennsylvania, USA
President, Team PHenomenal Hope
Team mates from Team PHenomenal celebrate their achievements.

A short break for a photo with the Eiffel tower allows everyone a moment’s rest.

PHAware group running a marathon; one of 14 events across the world.

Lights, camera... Action!
Eileen Bauer (left) takes a picture with other fundraisers at the Team PHenomenal event

Picturesque views in the Southern Alps
Pulmonary arterial hypertension and aging: Is there a connection?

by Aleksandar Petrovic, Michael Seimetz, Argen Mamazhakypov, Oleg Pak, Akylbek Sydykov, Djuro Kosanovic

Prelude

Advanced age has been described as an important factor associated with various medical conditions, such as diabetes, kidney diseases, osteoporosis, arthritis, neurodegenerative disorders (Alzheimer’s and Parkinson’s diseases) and different cardiovascular alterations (atherosclerosis and hypertension) (1-3). In addition, available literature has indicated the existence of the “physiological aging of the respiratory system” and development of the lung parenchyma structural changes which may be characterized as emphysema-like (4). With regard to the pulmonary circulation, it has been revealed that pulmonary artery systolic pressure increased in healthy elders compared to the younger individuals, suggesting the presence of the “physiological aging of the pulmonary vascular system” (5-7). However, what does it mean for the development of pulmonary arterial hypertension (PAH)? Importantly, the recent intriguing findings postulated a clear shift from our previous point of view of PAH as a disease of younger females to a disease of older patients with no sharp difference in gender distribution (8-11). In order to identify and precisely delineate the potential role of aging in the pathology of pulmonary hypertension (PH), with the main focus on group 1 (12), we would like to start this interactive discussion among those interested in this topic. Our brief discussion will serve just to scratch the surface of this complex clinical and scientific issue.

Main Article

Accumulated evidences from the scientific and clinical literature sources clearly indicated that the ultimate (and still unavoidable) effects of aging are “visible” at all levels of organism’s biology, starting from the whole body, organs and tissues up to the cellular and molecular dimensions (13, 14). For example, “molecular aging” may be reflected by fact that there is an accumulation of the reactive oxygen species (ROS) over time, which may lead to the subsequent ROS-induced damage of the essential macromolecules, such as DNA, proteins and lipids (14). At the cell level, it has been suggested that the cellular senescence represents an important event crucially associated with age (1, 13). Even more, this process is sometimes called as “cellular aging” (13). In general, the cellular senescence is defined as an event when the proliferating cells achieve the state of permanent cell-cycle arrest, and this phenomenon is characterized by a significant alteration in “normal” cell morphology, physiology and behavior (1, 13). Several different triggers apart from the historically known telomere shortening, including DNA damage, oncogene signals and oxidative stress, have been identified (1, 13). Despite these advances in the knowledge, it still remains unresolved how exactly the cellular senescence contributes to the development of age-related diseases.

With regard to the cardiovascular disorders, it is known for a long time that these diseases, including atherosclerosis and hypertension, are associated with aging and such age-induced pathological events consider endothelial dysfunction, vascular remodeling and disorganized angiogenesis (1). The detailed description about the characteristics of endothelial (ECs) and vascular smooth muscle cell senescence and its potential connection with altered miRNA signaling in orchestrating the cardiovascular pathologies is nicely reviewed in the paper from Schraml and Grillari (1). Furthermore, an intriguing summary from Lakatta’s review article indicated enhancement of various signals and events which occur in humans over 65, such as pro-inflammatory and oxidative stress-related mediators (transforming growth factor-β, monocyte chemoattractant protein-1, nicotinamide adenine dinucleotide phosphate oxidase, tumor necrosis factor-α...),
matrix metalloproteinases and dysregulated cellular processes including endothelial dysfunction, intimal thickening, proliferation and migration (3). All people working in the field of pulmonary vascular research have already recognized that these signaling molecules and cellular events are also important players in development of pulmonary vascular remodeling and PAH (15-21).

Finally, focusing to the field of pulmonary vasculature and cellular senescence, some interesting findings have been demonstrated in the context of PH associated with chronic obstructive pulmonary disease (COPD), a lung disease known to be *eo ipso* age-dependent and characterized by telomere shortening (22, 23). The authors revealed that pulmonary artery smooth muscle cells (PASMCs) senescence is indeed a significant player in pulmonary vascular remodeling process, a hallmark of PH (22). Based on this knowledge, one can expect that senescent PASMCs may have similar properties and functions in development of PAH as compared to the lung disease associated PH, since many pathological events and features that underlie remodeling process are shared between different PH forms (24). Therefore, future research is crucially needed. Another interesting aspect is the potential involvement of dysregulated caveolae (invagination of the membrane, rich in cholesterol and sphingolipids) and its structural protein caveolin-1 in age-related cardiovascular pathologies, including PH/PAH (25-29). The contribution of caveolin-1 to the pathology of PAH is very complex story, and this protein actually may exert compartment-specific opposite role in disease development and progression, dependent on the pulmonary vascular cell type involved (ECs versus PASMCs) (26-29). In the end, since the right heart failure is the ultimate pathological event of this severe pulmonary vascular disease, it is worth noting that aging healthy subjects and PAH patients show some similarities with regard to the right atrial function, compared to the younger healthy subjects and non-PAH controls, respectively (30).

**The question for interactive discussion**

Based on the above described scientific and clinical facts, ideas and suggestions, we would like to postulate the following question:

*Is there a connection between pulmonary arterial hypertension and aging?* Our question is directed to all scientists, clinicians and others interested in this topic across the world to try to answer and expose their own views, perspectives and visions in the next volume/issue of the PVRI Chronicle.

**References**


Our new website is now live.

We’ve been looking forward to showing you this all year. The new PVRI website is now live and ready for you to use. With our members base featuring over 800 scientists, pharmacologists and regulatory bodies, there's never been such a great time to join the PVRI and help shape the future of treatment for Pulmonary Vascular Disease.

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Hypoxic pulmonary hypertension: hypoxic pulmonary vasoconstriction vs. vascular remodeling

by Argen Mamazhakypov, Abdirashit Maripov, Kabita Pradhan, Aleksandar Petrovic, Oleg Pak, Michael Seimetz, Djuro Kosanovic, Akylbek Sydykov

PRELUDE

Hypoxic pulmonary vasoconstriction (HPV) is a unique response of the pulmonary vessels to alveolar hypoxia. In global alveolar hypoxia, however, HPV involves the entire pulmonary circulation resulting in increased pulmonary vascular resistance (PVR). Chronic global alveolar hypoxia is accompanied by structural remodeling of pulmonary vessels, which has long been thought to play a major role in the persistent elevation of PVR in chronic hypoxia-induced pulmonary hypertension (PH). However, more recent studies provided evidence that persistent vasoconstriction is an important contributor to chronic hypoxic PH. Furthermore, recent studies using genetic mouse models clearly demonstrated that different mechanisms regulate pulmonary vascular responses to acute, sustained and chronic hypoxia. In order to identify and precisely delineate the contribution of HPV and vascular remodeling to chronic hypoxia-induced PH we would like to initiate this interactive discussion among those interested in this topic.

MAIN ARTICLE

For most mammals, including humans, ascent to or residence at high altitude is associated with an increase in pulmonary artery pressure (PAP). The initial rise in PAP on exposure to high altitude hypoxia is due to acute hypoxic pulmonary vasoconstriction (HPV) (1). It is generally accepted that acute HPV is an adaptive response of the pulmonary circulation to a regional alveolar hypoxia, which diverts blood flow from poorly ventilated to optimally ventilated lung segments thereby optimizing ventilation-perfusion matching and gas exchange, though it might merely represent a vestige of fetal pulmonary physiology (2, 3). Nevertheless, acute HPV in local alveolar hypoxia is limited to the affected lung segments and is not accompanied by increase in PAP. In global alveolar hypoxia, which occurs at high altitude, however, HPV involves the entire pulmonary circulation resulting in increased pulmonary vascular resistance (PVR).

In humans, pulmonary vascular response to acute hypoxia has two distinct components: a rapid vasoconstriction occurring within a few seconds with maximal elevation in PAP at 15 min, followed after about 40 min by a secondary, more gradual increase in PAP, reaching a plateau at 2 hr and lasting for at least 8 hr (4, 5). Similarly, in isolated buffer-perfused rodent lungs and isolated pulmonary artery rings, hypoxia elicits a biphasic response consisting of a transient vasoconstriction lasting about 10–15 min, followed by a sustained constriction that develops more gradually to reach a plateau after 30–40 min (6, 7). Variation in the pulmonary vascular response to acute hypoxia is well documented, both between and within species (2, 8). In humans, extreme responders with an exaggerated HPV might be at risk of presenting acutely on arrival at altitude with high-altitude pulmonary edema (HAPE), a potentially fatal noncardiogenic pulmonary edema (9). Indeed, numerous studies have shown that HAPE-susceptible subjects have a significantly greater increase in PAP in response to acute hypoxic exposure (9-11). Remarkably, longer duration of the acute hypoxic exposure (2 hr vs. 15 min) at low altitude is associated with less overlap between HAPE-susceptible and HAPE-resistant subjects (12).

Chronic global alveolar hypoxia also evokes structural remodeling of pulmonary vessels characterized by increased muscularization of
Hypoxic pulmonary hypertension: hypoxic pulmonary vasoconstriction vs. vascular remodeling

smooth muscle cells into previously non-muscularized arterioles (13). This vascular remodeling has long been thought to play a major role in the persistent elevation of PVR in chronic hypoxia-induced PH as earlier studies have shown the lack of responsiveness to breathing oxygen at high altitude to reverse the rise in PVR in acclimatized lowlanders and high altitude residents (14-16). However, more recent studies provided evidence that persistent vasoconstriction is an important contributor to chronic hypoxia-induced PH (17). It was shown that vasoconstrictor and structural mechanisms contribute equally to chronic hypoxia-induced PH in mice (18). In contrast, persistent vasoconstriction, rather than structural changes in the vasculature, is the main underlying mechanism of increased PVR in chronic hypoxia-induced PH rats (19, 20). An interesting observation on the relative contribution of vasoconstrictor and structural mechanisms to chronic hypoxic PH was made in cattle (21). After several months spent at high altitude, administration of oxygen to a steer with moderate PH reduced PAP to near normal values, whereas in a steer with severe PH led to only a partial reduction of PAP.

Although it is generally assumed that chronic exposure to hypoxia leads to development of hypoxia-induced PH, not all individuals and not all high altitude ethnic groups are prone to elevated PAP and develop pulmonary vascular remodeling (22-24). For example, Tibetans and Sherpas, who share recent ancestry with the Tibetan highlanders (25), have been reported to have the lowest mean PAP at rest and display no rise in PVR at high altitude (26-28). Moreover, small pulmonary arteries of native Himalayan highlanders are thin-walled with no medial hypertrophy of the pulmonary arteries (29). Interestingly, sea-level Tibetans exhibit blunted pulmonary vascular responses to both acute and sustained hypoxia (30). In the first days of acclimatization to high altitude, Sherpas display lower PAP compared to lowlanders (28). However, no differences between high altitude Sherpas and fully acclimatized sea-level inhabitants have recently been reported (31). It would also be interesting to conduct direct comparisons of PAP between high altitude Tibetans and lowlanders with long-term residence at high altitude.

It has long been anticipated that the mechanisms underlying the pulmonary vascular responses during chronic hypoxia are the same or related to those to acute hypoxia. For example, lowland species with stronger acute HPV develop more severe PH in chronic hypoxia than animals with weaker HPV (3). In cattle, a correlation between strength of acute HPV and severity of chronic hypoxia-induced PH has been observed (32). Interestingly, susceptible calves display pulmonary medial hypertrophy even before their exposure to chronic hypoxia (33). In a study of Kyrgyz high-altitude residents 10-year follow-up revealed progressive increase of PAP in those with an exaggerated HPV and no change in normally responsive highlanders (34). However, no correlation between the magnitude of the acute HPV and the severity of chronic hypoxia-induced PH was observed in other species. For example, though coatis have a vigorous acute HPV (35), they do not develop PH and right ventricular hypertrophy (RVH) in response to chronic hypoxic exposure and do not display muscularization of pulmonary arterioles (36). On the contrary, despite a relatively weak HPV response to acute hypoxia in guinea pigs, they develop chronic hypoxic PH with structural remodeling of pulmonary vessels and RVH (37).

Recent studies using genetic mouse models clearly demonstrated that various signaling pathways regulate pulmonary vascular responses to acute, sustained and chronic hypoxia (38-40).
For example, TRPC6-deficient mice display sustained HPV and chronic hypoxia-induced PH with pulmonary vascular remodeling despite disrupted acute HPV (39). In contrast, TRPC1 disruption does not impair the acute HPV while diminish development of pulmonary vascular remodeling in chronic hypoxia (38).

In summary, HPV plays a pivotal role in the pathogenesis of HAPE. New evidence suggests that pulmonary vasoconstriction may play an important role in chronic hypoxia-induced PH. Successful adaptation to life at high altitude might involve genetic adaptation of the different signaling pathways regulating pulmonary vascular responses to acute, sustained and chronic hypoxia.

The question for interactive discussion

Based on the above described scientific and clinical facts, ideas and suggestions, we would like to postulate the following question: what is the relative contribution of acute and sustained HPV and vascular remodeling to chronic hypoxia-induced PH in humans? Our question is directed to all scientists, clinicians and others interested in this topic across the world to try to answer and expose their own views, perspectives and visions in the next volume/issue of the PVRI Chronicle.

References


E-CIGARETTES: A FAIRY TALE OF A HEALTHY ALTERNATIVE TO CONVENTIONAL CIGARETTES?
by Elsa Tadele, Djuro Kosanovic, Akybek Sydykov, Srikant Karnati, Michael Seimetz

PRELUDE

Smoking of conventional cigarettes with tobacco is known as a cause of severe health problems worldwide, amongst others including chronic lung diseases and cancer. One reason for the high incidence of smokers is the fact that people become addicted to the cigarettes in which it can be debated if the addiction is physically or mentally based. Anyway, there is no doubt that cigarettes are harmful and that smoking cessation is of high importance for smokers who are not ill and even more for patients who already suffer from the consequences of long-term smoking, such as chronic obstructive pulmonary disease (COPD). It has been demonstrated that smoking cessation has beneficial effects on life quality. However, it is difficult for smokers to quit. To help them, a variety of nicotine replacement products have come to the market including nicotine patch, gum, inhaler, lozenges and nasal spray – and recently e-cigarettes. When e-cigarettes first appeared, they were promoted as a non-hazardous alternative to conventional cigarettes although containing nicotine. They are currently a hot topic for both smokers and scientists/clinicians. Increasing number of chronic and amateur smokers are using e-cigarettes and even some clinicians suggest them as a replacement therapy to conventional smoking. Despite the lack of long-term effects of e-cigarettes, they are freely available, even for adolescents. However, there is increasing evidence that e-cigarettes cause similar problems to conventional cigarettes. On the other hand, it is still debatable that e-cigarette smoking will actually help quitting conventional
smoking. This interactive discussion aims to challenge scientists, clinicians and other persons who are interested in this field to think about the usefulness of e-cigarettes, the pros and cons.

**Main Article**

E-cigarettes, first marketed in China in 2004, were introduced to the international market in 2007. Awareness and usage of e-cigarettes has drastically increased since entering the market. From the scientific point of view, it was surprising that the introduction of e-cigarettes took place so easily. They contain nicotine and artificial liquids and no long-term studies were available. The majority of e-cigarette users are smokers who anticipated that they are less toxic than conventional cigarettes and help them for smoking cessation.

An online survey of smokers who had tried e-cigarettes with an aim to assess the effectiveness of e-cigarettes as a smoking cessation tool with 222 respondents showed that 31% of respondents did not smoke cigarettes for 6 months from the time they started using e-cigarettes. This study also showed that 66.8% reduced usage of the number of cigarettes(1).

Another prospective study was performed on 40 smokers who were not thinking of quitting. After following the participants for six months, the study has shown a 50% reduction in the number of cigarettes smoked per day in 55% of participants without significant withdrawal symptoms(2). However, most of efficacy studies are short-term. The effectiveness of e-cigarettes as a smoking cessation tool in long-term still should be addressed. These studies might show reduction/cessation of cigarette smoking but we should not forget the big picture here with using e-cigarette that its main ingredient nicotine (an addictive substance and the main cause of addiction to tobacco) can lead to addiction.

Furthermore, e-cigarettes can cause acute effects comparable with conventional cigarettes. Right after a 42 years old woman started using e-cigarettes, she started having respiratory symptoms like dyspnea, productive cough and subjective fever. Seven months after the onset of her symptoms she was diagnosed with exogenous lipoid pneumonia which is uncommon, primarily chronic inflammatory reaction resulting from continuous aspiration of oil substance(3).

Moreover, a 20 years old healthy man had persistence cough, shortness of breath and facial flushing one hour after vaping an e-cigarette. After a series of clinical examinations he was diagnosed with acute eosinophilic pneumonia (a rare condition characterized by rapid accumulation of eosinophils in the lungs as a consequence of unidentified, nonspecific triggering agents)(4).

A laboratory-based intervention study...
analysed oxidative stress and lung function in 40 participants divided into two groups (30 individuals in experimental and 10 in control group). The experimental group was provided with e-cigarettes and was using e-cigarettes only for 5 min. The level of fractional exhaled nitric oxide [FENO] (a quantitative, noninvasive and safe method of measuring airway inflammation that provides a complementary tool to other ways of assessing airways disease) was assessed before and after e-cigarette usage. FENO was significantly decreased in experimental group after using e-cigarettes. The study also shows using impulse oscillometry increased airway impedance and peripheral airway resistance in experimental group compared to control group(5).

In another study, the potential effects of e-cigarettes vapor on cardiomyoblast cell viability was evaluated. They extracted the vapor from 20 different e-cigarette liquids with different flavoring substances and exposed the cells to different concentrations for 24 hours. Four out of 20 e-cigarettes showed cytotoxic effects on cardiomyoblasts. Moreover, the study addresses whether e-cigarettes are less harmful than that of conventional cigarettes and indicates that e-cigarette vapor extracts were less cytotoxic compared to cigarette smoke extract on cultured cardiomyoblasts(6).

Another study by Bahl and colleagues evaluated the cytotoxicity ability of 35 different flavored e-cigarette liquids on human embryonic stem cells (hESC), mouse neural stem cells (mNSC), and human pulmonary fibroblasts (hPF). They treated the cells with different concentration of refill liquids and evaluated cell cytotoxicity. Except one (Bubble-gum) all refill liquids were cytotoxic to the cells to various extent. The cytotoxicity of refilled solution mostly depends on the dose of refill solution and flavors as well as cell type (stem cells from embryos (hESC) and new born (mNSC) were more sensitive to refill solutions than adult lung fibroblasts)(7).

Vegetable glycine (VG) and propyl glycol (PG) go through decomposition at high temperature into low molecular carbonyl compounds such as the carcinogens formaldehyde and acetaldehyde. Using high-performance liquid chromatography and a diode array detector Kosmider et al. measured the amount of carbonyl compounds in e-cigarettes vapor. Vapor extract collected from 70ml volume of puff a total of 15 puffs from ten different commercially available e-cigarette liquids, formaldehyde and acetaldehyde release were detected in 8 of vapor extract. However, the amount of released substances was affected by battery output voltage (the higher the voltage the higher the amount of carbonyl compounds released) (8).

Frighteningly, although nobody knows about long-term effects and risk of addiction, teenagers are currently allowed to use e-cigarettes unrestrictedly. However, based on recent observations, a number of countries are considering to prohibit the easy access of e-cigarettes for young people. A recent study by Lauren Dutra and Stanton A. Glantz used data from the Centers for Disease Control and Prevention (CDC) to demonstrate that use of e-cigarettes is often associated with cigarette smoking among adolescents. E-cigarette use recently doubled among adolescents in the United States, from 3.3% in 2011 to 6.8% in 2012. The authors used a nationally representative sample of over 38,000 U.S. middle and high school students. They showed that adolescents who used e-cigarettes were more likely to be cigarette smokers and more likely to progress from experimenting with cigarettes to become regular cigarette smokers. E-cigarette users,
despite having higher reports quit smoking than non-e-cigarette users, were less likely to have stopped smoking cigarettes and were heavier cigarette smokers. These results call into question e-cigarette advertisers’ claims that e-cigarettes are effective smoking cessation devices and questions whether e-cigarette use could actually contribute to cigarette smoking not only among teens (9), but also among adults.

At the annual congress of the European Respiratory Society (ERS) in Amsterdam 2015, e-cigarettes were a hot topic. There were some studies from animal models showing that e-cigarettes containing nicotine cause acute inflammatory response similar (or comparable) to that of conventional cigarettes. There was an interesting oral presentation about a retrospective view at hitherto clinical studies which tried to find out if e-cigarettes can help people to quit smoking. Interestingly, analyzing the data and study designs, the presenter concluded that in most cases e-cigarettes do not help quitting smoking but just lead to a shift from conventional to e-cigarettes. Even more often, respective people just mix between these two kinds of cigarettes. One comment from the audience during this presentation was remarkable which was in turn: “Originally, e-cigarettes were developed and introduced by the tobacco smoke industry, an industry which spent a lot of effort to make users of cigarettes addicted. Do you really believe that the same industry now wants their customers to get rid of smoking?”. Having this in mind, the outcome of studies investigating the safety and benefit of e-cigarettes in comparison to conventional ones will be of interest.

In conclusion, the idea to invent innovative solutions which can help people to stop smoking is eligible. However, the realization should be sophisticated and most notably scientifically approved and honest. It is not acceptable claiming such an alternative will be healthy, non-hazardous for adolescents and adults, and not addictive if this is not proven accurately because this is playing Russian roulette with people’s health and in particular with the future of our children. Maybe e-cigarettes helped some people to quit smoking, but in many cases it seems that there is just a shift from conventional to e-cigarettes. Finally, more rigorous studies are required to understand the significant benefit of e-cigarettes in contrast to existing smoking cessation tools. Maybe the industry reacts to recent data in a way that they focus on e-cigarettes not containing addictive substances such as nicotine. Because it is likely that such e-cigarettes could help some people to quit smoking by mimicking the ritual of smoking.

**The question for interactive discussion**

1) Are e-cigarettes a useful tool for smoking cessation?
2) What about the easy access of e-cigarettes to our children/adolescents? Do we support the risk for them of getting smokers by just not taking into account that e-cigarettes may be harmful mediators and ignoring the recent data respectively?
3) Are there real measurable advantages of e-cigarettes compared to conventional cigarettes or other smoking cessation tools?

We would like to invite all experts and other persons interested in this field to reply and express their views on this topic, in the next volume of PVRI Chronicle.
Prevalence and hospital discharge status of human immunodeficiency virus–associated pulmonary arterial hypertension in the United States

http://www.jstor.org/stable/10.1086/682222

Prevalence of HIV-PAH

<table>
<thead>
<tr>
<th>Database</th>
<th>Prevalence</th>
<th>By Race</th>
<th>By Sex</th>
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<tbody>
<tr>
<td>NVSS</td>
<td>0.15%</td>
<td>↑ White</td>
<td>↑ ♂</td>
</tr>
<tr>
<td>NHDS</td>
<td>0.04%</td>
<td>↑ AA</td>
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Lower prevalence of HIV-PAH at discharge suggests a potential lack of clear screening guidelines which could put individuals with HIV-PAH at risk for poorer outcomes due to late or missed diagnosis.

Rebecca Vanderpool
University of Pittsburgh Medical Center
Pittsburgh
United States
Tetraspanins (TSPAN) are cell surface proteins and the family contains 34 members in eucaryota (TSPAN1-34) [1, 2]. Tetraspanins are relatively small proteins in the range of 22-30 kDa and are present in nearly all mammalian cells and many species such as Schistosoma, C. elegans and Drosophila [2].

Each protein consists of four conserved transmembrane domains: characteristic large extracellular loop and short cytoplasmic domains. Extracellular loop contains CCG motif (Cys-Cys-Gly) and most of tetraspanins contain two or four additional Cys residues [2-4]. Tetraspanins do not have any activity nor function as classical cell membrane receptors. However, they serve as an anchor to organize interaction and attachment of other tetraspanins, molecules, proteins, receptors, etc. as well as organization of various membrane complexes. It was reported that they play a role in tissue differentiation; egg-sperm fusion; tumor-cell metastasis; cell proliferation, adhesion and migration; interactions with integrins, matrix metalloproteinases (MMP), growth factor receptors and immunoglobulins [4-9].

Growth factors play an important role in pathogenesis development of pulmonary hypertension [10-12] and tetraspanins were reported to regulate their receptors and signalling in cancer cells. Transforming growth factor beta (TGF-β) signalling [13] was affected when tetraspanin CD151 was depleted. Cell migration, proliferation and metastasis were significantly reduced as well as scattering was induced [13]. Moreover, TGF-β1- and growth factor-mediated signalling activities modulate tetraspanin TM4SF5 expression which leads to acquisition of mesenchymal cell features, suggesting that TM4SF5 induction may be involved in the development of liver pathologies [14]. Additionally, some reports show that tetraspanin CD63 serves as a bridge between β1 integrin and VEGF-R2 [15]. Moreover, a study by Choi et al. suggests that tetraspanin TM4SF5 and IGF1-R are able to modulate one another and each protein promoting the expression of the other [16].

Tetraspanins have been shown to interact with different members of integrins. These interactions regulate cell adhesion, migration, signalling and crosstalk with extracellular matrix and adherent junctions which as a result induce tumor invasion, metastasis and progression [4-7].

Tetraspanin family is well recognized and investigated in cancer. However, despite importance and function of tetraspanins in many diseases, there are no reports so far regarding them in pulmonary hypertension. As described above targeting tetraspanins offers attractive novel therapeutics to attenuate cancer changes.

**References**

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Systemic Lupus Associated Pulmonary Hypertension
by Mamotabo Matshele

Abstract
Systemic lupus erythematosus (SLE) is an autoimmune disease frequently associated with pulmonary and cardiovascular complications in humans, even in the absence of associated or concomitant connective tissue disease. Nevertheless, the effects of SLE on the pulmonary vasculatures have not been extensively studied or reviewed. Pulmonary hypertension (PH) is one of severe manifestations of (SLE). Due to improvement in the current understanding of the pathogenesis and pathology of these diseases, improved methodology in the conduct of advanced research and advancement of successful medical, and surgical therapies; our understanding of SLE associated PH has evolved dramatically. In this paper we will review the previous and current evidence regarding the prevalence, clinical parameters, prognostic implications and survival rates in SLE associated PH. Accordingly, we will review and contrast the association between these two conditions, highlighting the clinical features, discussing the methodological limitations of existing data on prevalence, treatment options and survival; and draw special attention to special situations, in particular pregnancy.

Introduction
Systemic lupus erythematous (SLE) is an autoimmune diseases and is associated with pulmonary and cardiovascular complications. Even though pulmonary hypertension (PH) has less often been reported as one of the manifestations in SLE patients, both invasive and non-invasive exercise hemodynamics have been previously reported to be abnormal in these patients [1, 2]. Majority of patients with SLE present with marked decrease in exercise capacity compared with normal individuals [1, 2]. The exercise intolerance in these patients could be multifactorial as they do present with easy fatigability, physical deconditioning, musculoskeletal and neurological abnormalities, which poses challenges when managing patients with SLE [3, 4].

In addition to cardiopulmonary complications of SLE, the five criteria of pulmonary hypertension based on the current World Health Organization classification have been reported [5, 6]. Pulmonary hypertension in SLE patients may also occur as a result of concomitant pulmonary diseases, and it could also result from associated pulmonary vasculitis and chronic thrombotic diseases.

Prevalence
Although the prevalence of PH in SLE patients could be variable, previous studies reported the prevalence of PH in these patients to be ranging between 0.5% and 45%, however these are old studies [7 -12, 13- 16]. However, some recent studies have estimated the prevalence of SLE associated PH to be below 20% [17-19]. The pivotal factor leading to this wide variation is the diagnostic method used to evaluate the magnitude of pulmonary arterial systolic pressure in these patients. In addition, the variation could be related to inadequate information provided in regards to the underlying etiology of the PH. Despite these pitfalls, the association between SLE and PH or SLE associated PH seems to be increasing over time. Serial echocardiographic studies have demonstrated an increase in prevalence of PH; with reported prevalence rising from 14% to 43%
over 3-5 years of follow-up period [1, 11].

**Clinical demographics and risk factors**

Clinical manifestations of SLE associated PH vary, however the commonly reported features in these patients include insidious onset of dyspnea, easy fatigability, cough and chest discomfort. Unfortunately, these symptoms may develop late in the course of the disease. The pathological pulmonary vascular changes may be far more advanced by the time these patients present for their initial consultation with their primary physician, as a result SLE associated PH should be excluded in SLE patients presenting with these symptoms.

The characteristics of patients with SLE associated PH are similar to those of patients with idiopathic pulmonary arterial hypertension (IPAH), as a result it might be challenging to separate the two pathological entities during clinical evaluation. Even though there is no clear association between the duration of SLE and the development of PH, patients with SLE seem to develop PH within the first five years of the disease entity. Most interestingly PH may be the only sole clinical manifestation in some patients with SLE [20]. Some reports mentioned that there is no association between the presence of PH and degree, severity or activity of SLE based on the serology or activity markers; however this is very controversial as some reports have reported some association [7, 12, 21].

**Management:**

**Medical Treatment**

The treatment modalities for SLE associated PH are similar to those of IAPH which include: oxygen, anticoagulation, vasodilators and calcium channel blockers. Different therapeutic modalities have previously been tried in these patients with no individual therapeutic regimen shown to be superior to others in managing SLE associated PH [22-28]. Different vasodilators have been previously tried and proved to be effective in most patients, and these include both selective and nonselective endothelin receptor inhibitors, phosphodiesterase-5-inhibitors, and different prostanoids regimens [1, 22-28, 29-31]. Most patients with SLE associated PH receiving vasodilators demonstrated significant improvement in terms of New York Heart association Functional Class, exercise capacity, quality of life and delayed diseases progression [29-31]. Clinical and sustained hemodynamic improvement has been reported after intensive immunosuppressive therapy which includes a combination of intravenous cyclophosphamide and high tapering doses of oral glucocorticoids [32-34].

**Surgical Options**

The surgical options for the management of SLE associated PH are similar to those used for other types of PH in patients who have failed optimal medical therapy. Atrial septostomy, lung or a combination of heart-lung transplantation are options in some patients with SLE associated PH. The main limitation for considering the surgical intervention in SLE associated PH is multiorgan involvement from the systemic disease and complications from the underlying co-morbidities which deem most patients unsuitable for surgical intervention. Although IAPH has been reported to have a better prognosis compared with SLE associated PH, some patients with SLE associated...
PH, some patients with SLE associated PH do much better if treated early [35-36].

**Survival**

One- and three-year survival rates for SLE-associated PH have been reported to be 78% and 74% respectively [37-38, 21]. However a one-year survival rate has been reported above 90% and this improvement has been attributed to early introduction of advanced medical therapy which includes immunosuppression [39-40, 21]. Despite these advancements, if other respiratory disorders coexist with PH, the prognosis remains poor in these patients. Despite advancement in medical therapies the survival rate for IAPH remains better compared with SLE associated PH. The prognosis is much worse for those with concomitant respiratory disorders.

**Special situation**

One special situation which needs special attention is pregnancy. Pregnancy should be discouraged in patients with SLE or SLE associated PH, as pregnancy can exacerbate underlying SLE and it is also recommended as an absolute contraindication in patients with PH [1, 41]. SLE associated PH has been reported to be common among women of child bearing age, and for that reason pregnant mothers should be screened for PH as the maternal mortality is quite high in this group [42-43]. The maternal mortality secondary to SLE associated PH has been reported to be extremely high, even higher than that related to any other pulmonary vascular disease in pregnancy [42-45].

**Conclusion**

Although recent studies have reported better survival in SLE associated PH due to the introduction of advanced medical therapy, SLE associated PH is generally associated with high mortality rates [35-36]. Due to these reported data on poor outcomes in this population, pregnancy should be discouraged in women of childbearing age with SLE or SLE associated PH; and therefore it should be mandatory to recommend screening for SLE or SLE associated PH in women of child bearing age.

**References**

Learner’s Corner

Pulmonary Hypertension in Constrictive Pericarditis or Systemic Lupus Erythematosus Patients?


Learner’s Corner

Pulmonary hypertension in Constrictive Pericarditis or Systemic Lupus Erythematosus patients?


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Interview with Dr. Buddha Basnyat: High altitude physiology and medicine and potentiality of conducting high altitude research in Nepal

by Himal Luitel & Matiram Pun

General Introduction

Prof. Buddha Basnyat lives in Kathmandu, Nepal and is the current president of International Society of Mountain Medicine (ISMM). He is one of the leading experts in mountain and travel medicine around the world. He has been actively involved in the researches and academic mentoring of graduate students in high altitude and travel medicine as well as infectious diseases (e.g. enteric fever, hepatitis and undifferentiated febrile illnesses).

After undergraduate schooling in Nepal, he was trained in medicine in the Punjab, India and then completed masters in respiratory physiology at the University of Calgary, Canada, and an internal medicine residency at the Banner Good Samaritan Hospital in Phoenix, Arizona, USA.

After completing studies in North America, Dr. Basnyat returned to his home country Nepal.

Currently, he is a consultant at Patan Hospital and leads the Oxford University Clinical Research Unit- Nepal (OUCRU-Nepal) based at that hospital. For over a decade he was the professor of physiology at the Maharajgunj Medical Campus, Institute of Medicine (IOM), Tribhuvan University Medical College in Kathmandu. He is now a professor of physiology at the Patan Academy of Health Sciences (PAHS). He is also a Fellow of the American College of Physicians and a Fellow of the Royal College of Physicians, Edinburgh.

He leads Mountain Medicine Society of Nepal (MMSN) and inspires young Nepali doctors and medical students to get involved academic field of medicine with a special focus in Mountain Medicine and Infectious Diseases. Dr. Basnyat takes great pleasure in working with and helping young clinicians in the study of high altitude illness and undifferentiated febrile illness in the tropics, both common but neglected problems in Nepal. He is also the Medical Director of both
High altitude medicine but because Nepal has many infectious diseases, I got interested in this too. More people are affected by infectious diseases like typhoid than high altitude illness so hypoxia studies seem almost like a luxury in comparison (except when it pertains to the millions of poor pilgrims with comorbidities who trudge up the mountain to reach the sacred site). Something has to be done for them in “Bharat Barsa” (South Asia). Maybe Modiji(current Prime Minister of India) can help out with his spiritual drive and government support? 

Q3. As you are extensively involved in high altitude research, may you elaborate the high altitude related pathologies and their research in Nepalese context?

Dr Basnyat: We do mostly quite basic, inexpensive research like doing simplerandomized controlled trials (RCTs) of different Diamox dosages to see what low dose is effective or to see if non-steroidal anti-inflammatory drugs (NSAIDs) or Tylenol (Acetaminophen) is effective. Very seldom we do molecular stuff but this is always collaboration.

Q4. You have primarily focused on acute altitude illnesses. Do you think there is scope for chronic altitude illnesses in Nepal?

Dr Basnyat: The sample size would be very small I think. (Note from Editors: Dr Basnyat refers to the very low prevalence of chronic mountain sickness in Nepal Himalayas especially among Sherpas at the moment).

Q5. May we discuss the possibilities of basic and clinical research in high altitude related pathologies and international collaborations to increase the impact value of the findings??

Dr Basnyat: This would be a great idea but we need young people to be involved who have studied abroad and can use this (Western exposure) as a tool to help themselves and the many others.

Q6. In your opinion, how is altitude research different from other fields of biomedical research?

Dr Basnyat: This is a field research in Nepal so it comes with all the risks in methodology that a field research can suffer from and so we have to be clear about the limitations.

Q7. Is there scope and place for young scientists in Nepal?

Dr Basnyat: Yes there is. Who else but young scientists but they have to be innovative themselves. There is too much veneration of old age in our culture and although this is good, at times this can also be counterproductive for young people. Look at Nepal’s politics which is in shambles and one reason is too much following of old people.

Q8. How much support do you get from Nepal government for your research?

Dr Basnyat: Almost zero.

Q9. Can you make bread and butter working as a full-time researcher in Nepal?

Dr Basnyat: Probably not unless you do grant applications and apply abroad and can prove to them that you are a true research worker.

Q10. What do you think are the future avenues of altitude research?

Dr Basnyat: I think if young dedicated people get involved, the sky is the limit.

Q11. What would like to suggest young brains of Nepal who see you as a role model?

Dr Basnyat: Stick to your dreams and have faith in the “Brahma”. Try not to follow the crowd.
Try to help other researchers as much as you can and don't follow the cut-throat competition model of the Western world.

Dr. Himal Luitel PhD (1)
Dr. Matiram Pun (2) (3)

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Upfront dual combination therapy in a patient with polymyositis complicated by pulmonary hypertension
by Vikas Singh & M. Patricia George

Abstract:
A 62-year-old woman with a history of mixed connective tissue disease (MCTD) with polymyositis and Sjogrens syndrome presented as a challenging case of dyspnea and profound weakness with uncertainty as to whether her symptoms were due to polymyositis versus pulmonary vascular disease. In accordance with the AMBITION trail, she was started on combined endothelin-A receptor antagonist and phosphodiesterase type 5 inhibitor therapy with ambrisentan and tadalafil. The medications were well tolerated and her functional status was significantly improved in less than 3 months. This case report summarizes the upfront dual combination therapy in a patient with polymyositis complicated by pulmonary hypertension.

Case Synopsis
A 62-year-old woman with history of mixed connective tissue disease (MCTD) with polymyositis and Sjogrens syndrome presented for evaluation of dyspnea. Her functional status began worsening approximately 10-11 months prior to presentation and worsened around 6 months prior when she developed acute renal failure, etiology unclear, requiring plasmapheresis and hemodialysis. At presentation she was dyspneic even with minimal exertion. She was basically bed-bound with great fatigue at rest, and could barely get herself out of bed and ambulate, and endorsed 2-pillow orthopnea, paroxysmal nocturnal dyspnea and occasional dry cough and denied syncope or dizziness. Her physical exam was only significant trace pedal edema and decreased breath sounds in left lung base due to pleural effusion. CT Chest had shown nonspecific groundglass opacities scattered within the lungs and within areas of interstitial septal thickening suggestive of pulmonary edema. While pulmonary arterial hypertension (PAH) was at the top of the list on her initial presentation, there was also serious concern for severe polymyositis given her fatigue and profound weakness and poor follow up with her rheumatologist.

Pulmonary function testing (PFT) from 8 months prior had shown reduced DLco (40% predicted) with TLC 78% predicted. Her FEV1/FVC was 0.8 and FEV1 was 74% predicted. PFT and 6MWT could not be repeated due to her severe weakness. By echocardiogram at that time her estimated pulmonary artery systolic pressure (PASP) was 68mmHg. At the time of her referral visit, it had worsened to 107 mmHg. She underwent right heart catheterization which revealed right atrial pressure 11mmHg, mean pulmonary artery pressure (mPAP) of 45 mmHg with pulmonary capillary wedge pressure (PCWP) 7mmHg, cardiac output of 3.87 L/m by Fick, with a PVR of 8.8 Wood Units. Based on the AMBITION trial1 she was started on combined endothelin-A receptor antagonist and phosphodiesterase type 5 inhibitor therapy with ambrisentan, and tadalafil. She tolerated the medications well, and significantly improved her functional status in less than 3 months. Her WHO functional class improved from 3-4 to class 3, and she could now
walk in her home and was working with physical therapy on a regular basis to rebuild her strength.

Discussion: The idiopathic inflammatory myopathies (polymyositis, dermatomyositis and inclusion body myositis) are a group of rare connective tissue disease and can involve multiple organ systems. The lungs are the most commonly affected organs, occurring in more than 32-40% of polymyositis patients2-4. Interstitial lung disease is the most commonly reported complication, PAH could have prevalence up to 8% in anti-synthetase syndrome5. Post-mortem case reports have shown severe plexogenic pulmonary vascular disease changes6. The purpose of this case report is to highlight the patient’s presentation with severe deconditioning and subsequent response to dual upfront combination therapy in a case of MCTD with polymyositis with pulmonary hypertension.

References

Pulmonary Arterial Hypertension Associated with Scleroderma: The Patient’s Perspective

by H. James Ford

Introduction

The complexities and nuances of life for patients with pulmonary arterial hypertension and the associated treatment are not always fully explored during visits to the physician's office. The focus is rightfully on objective data, symptoms, and the results of diagnostic studies aimed at determining response to therapy and functional class. The interview below seeks to gain a fuller understanding of what life is like from the patient’s perspective on complicated, multi-modality treatment for PAH.

The patient interviewed below is a 72 year-old man with scleroderma-associated Group 1 PAH. He is married and lives with his wife. He has two grown children.

Tell me about your health and medical journey prior to being diagnosed with pulmonary arterial hypertension (PAH).

I had been pretty healthy most of my adult life. I did smoke cigarettes for about 25 years, but quit many years ago. In 1992, I began to develop lesions on my skin and my fingertips began turning white when exposed to cooler temperatures. I was referred to a rheumatologist and was diagnosed with telangectasias and Raynaud’s. The diagnosis given to me was CREST syndrome, a type of scleroderma.

I was told that no specific treatment was needed for this at that time. It didn’t really affect my lifestyle at all.

In 1998, I was diagnosed with diabetes. It was originally treated with oral medications, but in 2001, my endocrinologist put me on an insulin pump for continuous subcutaneous insulin infusion. Even that did not really slow down my lifestyle and it wasn’t too much trouble to manage.

When did you first develop symptoms of PAH?

In the second half of 2008, I began to experience slowly worsening shortness of breath and decreased energy level. It got to a point that I could not even go down the driveway to get the morning newspaper without becoming very out of breath. During a family vacation to the beach in early 2009, I was so short of breath I could hardly bend over or walk across the street. I had to have my son load up the suitcases in my car so I could return home.

I went to my primary doctor when I returned and he thought I had COPD since I used to smoke. He prescribed me an albuterol inhaler. I used this for about a week and it did not help much at all. I had an appointment to see my endocrinologist and I mentioned the breathing trouble to him. He called a pulmonologist and got me an appointment to be seen the following week.

What did you think was wrong?

My mother died of congestive heart failure, so I thought I might have that. Interestingly, after I was diagnosed with PAH, I went back and looked at my mother’s death certificate and it also listed pulmonary hypertension as one of her problems. I am not sure if it was the same as my PAH.

What happened when you went to visit the pulmonologist?

The pulmonologist ran pulmonary function tests and did a 6-minute walk test. My pulmonary
function test did not show signs of COPD. My oxygen level dropped significantly during the walk test and I was placed on supplemental oxygen with ambulation and activity. At that point, they were concerned about PAH because I had scleroderma and there were no signs of significant COPD to explain my symptoms.

How was the diagnosis of PAH made?

My pulmonologist ordered an echocardiogram that showed changes in the heart concerning for pulmonary hypertension. I was then told I would need a right heart heart catheterization. I usually get nervous about procedures, but I was so glad that they might find the reason for my symptoms that I was not anxious about the catheterization at all. Once it was completed, my pulmonologist informed me that I did indeed have PAH.

What was the first treatment you received for PAH?

I was started on bosentan and it was ultimately increased to a dose of 125 mg twice daily. How did you feel after starting the bosentan? After about 3 months on bosentan, I felt slightly better, but I was still pretty limited by shortness of breath. I went to visit my pulmonologist for a follow up appointment and had another 6-minute walk test performed. This showed that I was able to walk 25 meters farther than the last time. I returned again another 3 months later and an echocardiogram was done to reevaluate my heart. I did not really notice any additional improvement on the bosentan at that time, and my walk test had not improved further at this visit. The echocardiogram showed that the right side of my heart looked much worse and there was now some fluid developing outside the heart.

Were there any changes made to your treatment at that time?

My doctor was very concerned at this point, and admitted me to the hospital to start on intravenous epoprostenol. This required a permanent catheter to be placed under my collarbone. I had to learn how to operate the infusion pump and mix the drugs and place them in the pump. In addition, the medicine had to be kept cool with ice packs. I was discharged home and was increasing the dose of the epoprostenol every 4 days. After about 8 weeks, I was at the dose my doctor wanted me to be. I was feeling much better at this point.

How did the next few years go in terms of your treatment and symptoms?

I continued on the epoprostenol and the bosentan. My echocardiograms and walk tests continued to improve. I still needed supplemental oxygen to ambulate. I was much less short of breath, but still wasn’t as functional as I used to be before my symptoms began in 2008. Did you have any side effects from the medications? Yes, that was one of the hardest things to deal with. I had a lot of nausea and diarrhea when I started on epoprostenol. My doctor treated the side effects and it helped keep them somewhat under control, but it was still very difficult to adjust.

Another problem that developed was that I started to have frequent nasal bleeding. This was likely due to oxygen drying out my nose and also the epoprostenol had started to make my platelet counts drop far below normal levels. Eventually this became such a problem that I was switched from epoprostenol to intravenous treprostinil.

Was your life any different on the treprostinil?

It was a little easier to manage in that it didn’t require ice packs. I still had many of the same gastrointestinal side effects but they eventually eased some. My platelet counts did increase and improve and I have had very few nasal bleeds since the transition.

Did you need to start any additional treatments for the PAH?

Yes. My echocardiogram was improving but was not quite normal. My walk test was also not at the distance
my doctor wanted as a goal for me. I was thus started on tadalafil 40 mg daily in addition to my other PAH therapies. My walk test improved another 25 meters about 4 months after starting this medication. My echocardiogram is now almost normal as well. My doctor also referred me to a pulmonary rehabilitation program. I now go three times weekly and exercise with the assistance of therapists and oxygen. I feel this has helped my functioning and energy level significantly. Interestingly, most of the patients in my rehab class have COPD, not PAH. This has made me realize how relatively uncommon PAH is.

Looking back, do you feel like you are in a better position now compared to when your symptoms began?

Yes. When I started having the shortness of breath, I became very discouraged and downhearted. I had just recently retired and was enjoying playing golf and doing activities with my family. I was afraid I would not be able to do any of those things again. While I still can’t really play golf, I can do other things I enjoy. Most notably, I am now able to get out and see my grandson play baseball, as well as do light work around my yard and take walks in my neighborhood. I feel much more hopeful about life at this time.

I have had the opportunity to attend local patient education symposia on PH as well and that has helped me to better understand my disease and also to see how others are struggling with it as well. I have also learned that there may be an implanted treprostinil pump coming out in the next year or so. I am excited to hear about this and hope I can receive treatment through this route.

I also enjoy going to the beach with my family 2-3 times per year. While it’s more complicated to travel now, I am grateful that I can at least make the trip. Overall, things have turned out much better than I expected. I am happy that I was diagnosed relatively quickly and that much attention and diligence was put into my care and follow-up.
ОЦЕНКА ПОСЛЕОПЕРАЦИОННОГО ПЕРИОДА У ДЕТЕЙ С ЛЕГОЧНОЙ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ

Абзалiev Куат Баяндыевич, Абзалиева Сымбат Абулхаировна, Тойбаева Айгерим Куатовна.

Резюме

Современные тенденции в диагностике и лечении такой нозологической группы, как врожденные пороки сердца, устанавливают высокую планку для детской кардиологии и кардиохирургии. Программа «Саламатты Казахстан» позволила внедрить мировые стандарты хирургической коррекции ВПС, а также протоколы терапии такого грозного осложнения ВПС, как ассоциированная легочная артериальная гипертензия у детей. За период 2008-2014гг. были диагностированы и направлены на оперативное лечение более 170 детей с врожденными пороками сердца (ВПС), осложненными ассоциированной легочной артериальной гипертензией у детей. За период 2008-2014гг. были диагностированы и направлены на оперативное лечение более 170 детей с врожденными пороками сердца (ВПС), осложненными ассоциированной легочной артериальной гипертензией у детей. Наиболее типичной для детей с умеренной степенью легочной гипертензии. Программа «Саламатты Казахстан» позволила внедрить мировые стандарты хирургической коррекции ВПС, а также протоколы терапии такого грозного осложнения ВПС, как ассоциированная легочная артериальная гипертензия у детей. За период 2008-2014гг. были диагностированы и направлены на оперативное лечение более 170 детей с врожденными пороками сердца (ВПС), осложненными ассоциированной легочной артериальной гипертензией у детей.

По результатам исследования, хирургическая коррекция лево-правого шунтирования крови с ассоциированной легочной артериальной гипертензией у детей, существенно меняет центральную гемодинамику. И в отдаленные сроки после выполненной операции восстановление функциональных показателей сердца и микроциркуляции малого круга кровообращения в большей степени характерно для больных с умеренной степенью легочной гипертензии. Ключевые слова: врожденный порок сердца, легочная артериальная гипертензия, эхокардиография.

Resume

Current trends in the diagnosis and treatment of congenital heart diseases (CHD), set the high bar for pediatric cardiology and cardiac surgery. The “Salamatty Kazakhstan” program allowed to introduce international standards of surgical correction of CHD, as well as therapy guidelines for severe complications of CHD such as associated pulmonary arterial hypertension (APAH) in children. During the period from 2008 to 2014 more than 170 children with congenital heart disease (CHD), complicated by APAH were diagnosed and operated. We performed a retrospective analysis of the cardiovascular system in the postoperative period, as well as assessment of long-term results after surgical treatment of CHD.

According to the study, surgical correction of left-right blood shunting with associated pulmonary arterial hypertension in children, changes the central hemodynamics. And in long term results, improvements of functional parameters of the heart and pulmonary circulation of the microcirculation is more typical for patients with moderate pulmonary hypertension.

Key words: congenital heart diseases, pulmonary hypertension, echocardiography.

За последние десятилетия в Республике значительно улучшилась диагностика врожденных пороков сердца (ВПС), являющийся основной причиной смерти детей первого года жизни и частота которой составляет 30% среди всех пороков развития. Данные мировой специализированной литературы
дemonstрируют развитие такого осложнения, как ассоциированная легочная артериальная гипертензия среди ВПС с лево-правым шунтированием в 32-59%. По этой причине ранняя диагностика легочной гипертензии и своевременная хирургическая коррекция имеет весьма актуальное значение.

Современный уровень развития детской кардиологии и кардиохирургии врожденных пороков сердца позволяет диагностировать и восстанавливать здоровье детей с врожденным лево-правым шунтированием крови в развитых странах. Это достигается совместным усилием кардиохирургов и детских кардиологов в том числе путем максимального использования всего арсенала современных медикаментов средств. Но, несмотря на значительные достижения в хирургической коррекции врожденных пороков сердца, у большинства детей сохраняются различные остаточные анатомические и/или функциональные нарушения после операции, нередко приводящие к различным осложнениям.

Профилактика послеоперационных осложнений коррекции ВПС у детей является стратегической задачей, поскольку данная патология имеет серьезный прогноз, как в отношении уровня качества предстоящей жизни, так и социальной адаптации больного. Разработка мер профилактики и распространение знаний о них могут снизить, а иногда и предотвратить формирование осложнений врожденного порока сердца у детей.

Материалы и методы исследования
Всего за период 2008-2014 гг. обследованы и направлены на оперативное лечение более 170 детей с врожденными пороками сердца (ВПС), осложненными АЛАГ. Нами был проведен ретроспективный анализ состояния сердечно-сосудистой системы в послеоперационном периоде, а также оценка отдаленных результатов послехирургического лечения ВПС. Девочек составило - (52,7%), мальчиков – (47,3%). Возраст детей с ВПС был от 8 мес. до 15 лет.

Кардиоваскулярная оценка в раннем и отдаленном послеоперационном периоде включала в себя такие критерии, как: клинические проявления сердечной недостаточности (одышка, тахикардия, вздутие и пульсация шейных вен, гепатомегалия, асцит, отеки на конечностях, гидробаланс), лабораторные показатели метаболических процессов (КЩС, биохимический анализ крови, мочи), инструментальное обследование (ЭхоКГ, ЭКГ, рентген, измерение ЦВД) и пр.

Результаты исследования
В раннем послеоперационном периоде, в соответствии с тяжестью перенесенных хирургических вмешательств, симптомы сердечной недостаточности возникали у всех пациентов. Однако, хотелось бы отметить развитие недостаточности по правожелудочковому типу в 62% (вздутие и пульсация шейных вен (64 пациентов), акцент и расщепление второго тона над легочной артерией (46 пациентов), увеличение печени (54 пациентов), отеки на ногах (8 пациентов), асцит (4 пациента). У 56 (47,9%) пациентов имело место снижение диуреза). По данным инструментальных методов исследования отмечено повышение центрального венозного давления в среднем до 13,6±2,1 мм.рт.ст. Развитие плеврита отмечено в 21 случае, перикардита в 8.

Clinical Corner
ОЦЕНКА ПОСЛЕОПЕРАЦИОННОГО ПЕРИОДА У ДЕТЕЙ С ЛЕГОЧНОЙ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ
По данным ЭКГ в 19 случаях констатировано нарастание признаков гемодинамической перегрузки правого желудочка сердца.

В раннем послеоперационном периоде у 24,6% детей развились различные нарушения ритма и проводимости сердца. У четырех больных в основном после хирургической коррекции ДМЖП и АВК развилась полная атриовентрикулярная блокада и у одного таксишистолическая форма мерцания предсердий. Синдром слабости синусового узла диагностирован у пяти прооперированных. В терапии назначалась противовоспалительная терапия наряду с лечением сердечной недостаточности, без ожидаемого эффекта. В итоге, была проведена имплантация электрокардиостимуляторов во всех перечисленных случаях. У одного прооперированного ребенка зарегистрирована сино-аурикулярная блокада I степени. Экстрасистолия имела место у двух пациентов. В динамике по данным ЭКГ у 9 детей исчезли признаки перегрузки правого предсердия. При этом амплитуда зубца R достоверно уменьшилась и в среднем составила 1,3±0,1 мм (р<0,05).

По данным ЭхоКГ у 24,6% детей констатировано снижение ФВ левого желудочка в среднем до 55,3±2,1%. Тогда как, несмотря на положительную динамику размеров правых отделов сердца, снижение давления в легочной артерии в результате устранения лево-правого сброса крови, падение насосной функции правого желудочка сочетается со снижением его сократительной способности. Причем динамика показателей отличалась в группах больных с различной степенью легочной гипертензии.

У детей I подгруппы (с незначительной легочной гипертензией) в ближайшем послеоперационном периоде показатели сократительной функции левого желудочка достоверно увеличились в большей степени за счет изменения показателей фазовой структуры систолы. ΔS через 1 месяц после операции составил 39,3±0,5% (р<0,05), что достоверно выше, чем в группе здоровых детей (36,7±0,5%). Отношение REP/ET уменьшилось до 0,39±0,01 (р<0,05) по сравнению с дооперационным значением - 0,43±0,01.

Po данным проведенного регрессионного анализа выявлено, что основные показатели глобальной сократительной функции миокарда левого желудочка (ФВ и ΔS) отрицательно коррелировали с периодом предизгнания (r=-0,36; р<0,02), отношением REP/ET (r=-0,45; p<0,005), REP/АТ (r=-0,35; p<0,03) и положительно с периодом изгнания (r=0,35; p<0,02). Диаметр правого желудочка сердца и легочной артерии уменьшились, но не достигли нормы.
сердца и легочной артерии с уровнем среднего давления в легочной артерии (r=0,45; p<0,009) и ОЛС (r=0,49; p<0,005). В результате хирургического восстановления целостности перегородки или перевязки протока показатели насосной функции правого желудочка резко уменьшились до нормальных величин. При этом СИ снизился до 4,2±0,1 л/мин/м² (p<0,001). Систолическое давление в полости правого желудочка сердца достоверно уменьшилось до 25,0±0,5 мм рт.ст. (p<0,001), но не достигло нормальных значений (p<0,05). Тогда как ДДПЖ через 1 месяц после операции не отличалось от нормы, составив 8,7±0,6 мм рт.ст. (p<0,05). При анализе фазовой структуры систолы правого желудочка наблюдалось укорочение периода изгнания (268,7±8,8 мс, p<0,001) и в результате увеличение отношения RE/ET до 0,41±0,03 (p<0,001), а RE/AT - до 0,98±0,06 (p<0,001), что указывает на снижение сократительной функции миокарда правого желудочка. Среднее давление в легочной артерии незначительно уменьшилось, в то время, как ОЛС достоверно увеличилось в среднем до 483,0±47,5 дин/с/см-5 (p<0,01). По нашим данным отношение RE/ET правого желудочка сердца находилось в прямой корреляционной связи со среднем давлением в легочной артерии (r=0,58; p<0,001) и ОЛС (r=0,48; p<0,006). По-видимому, отрицательная динамика ОЛС относительна, так как в раннем послеоперационном периоде отмечено резкое снижение МОК правого желудочка сердца, а ОЛС – отношение среднего давления к МОК. Через год после операции у детей с исходно незначительной степенью легочной гипертензии (I подгруппа больных) констатировано достоверное увеличение КДО левого желудочка до нормального объема (76,4±3,8 мл; p<0,05). Размеры левых отделов сердца и параметры фазовой структуры систолы по сравнению с данными ближайшего послеоперационного периода несколько улучшились, но не достигли нормальных значений. Миокардиальный индекс левого желудочка нормализовался и в среднем составил 0,36±0,04. Показатели сократительной функции левого желудочка (ФВ и ΔS) находились в обратной корреляционной связи с показателями фазовой структуры сердечного цикла отношением периодов RE/AT (r=0,67; p<0,01), а отношения периодов RE/AT в среднем по группе составило соответственно 0,31±0,03 и 0,74±0,07 (в группе контроля 0,32±0,01 и 0,76±0,03). Среднее давление в легочной артерии через год после операции практически не отличалось от нормальных величин (15,3±0,6 мм рт.ст.) и равнялось 17,8±2,0 мм рт.ст. При этом динамика отношения периодов RE/AT правого желудочка сердца также имела достоверную корреляционную связь с давлением в легочной артерии (r=0,65; p<0,02), а величина сердечного выброса правого желудочка сердца находилась в обратной
зависимости с величиной среднего давления в легочной артерии (r=-0,66; p<0,03) и ОЛС (r=-0,64; p<0,04).

В группе больных с умеренно выраженной легочной артериальной гипертензией (II подгруппа) наблюдалась очень похожая динамика послеоперационных изменений, но менее выраженная. В ближайшем послеоперационном периоде у данной категории больных отмечена только тенденция компенсаторного увеличения гемодинамической нагрузки на левые отделы сердца, повышение показателей насосной функции и сократительной способности миокарда левого желудочка сердца. Сердечный выброс правого желудочка соответствовал системному и равнялся 4,8±0,3 л/мин/м2. Значения систолического давления в полости правого желудочка сердца достоверно снизились и составили 29,6±1,8 мм рт.ст. (p<0,001), в то время как ДДПЖ не достоверно снизилось с 15,0±1,5 мм рт.ст. до 13,5±2,5 мм рт.ст. Все это способствовало тому, что полость правого желудочка и диаметр легочной артерии лишь незначительно уменьшились и составили соответственно 22,4 ± 2,8 мм/м2 и 28,1±2,5 мм/м2. При этом сократительная функция правого желудочка так же как в предыдущей группе в целом была снижена. Давление в легочной артерии, рассчитанное по данным фазового анализа систолы правого желудочка сердца в раннем послеоперационном периоде, практически не изменилось.

Через год после операции у пациентов II подгруппы наблюдалось восстановление основных показателей кардиогемодинамики. ЧСС уменьшилась и не отличалась от таковой в группе контроля (69,8±3,1 уд.в мин). Морфофункциональные параметры левых отделов сердца практически достигли нормальных значений. Сохранялись признаки гипертрофии стенок левого желудочка. Толщина МЖП и ЗСЛЖ были увеличены соответственно до 135,2±8,5 мм (p<0,01), периода предизгнания и времени выброса. В результате увеличение времени ускорения кровотока из правого желудочка до 135,2±8,5 мм рт.ст. (p<0,01), периода предизгнания и времени выброса. В результате отношение РЕР/ЕТ и РЕР/АТ были повышены и соответствовали 0,45±0,06 и 0,93±0,09.

У детей с высокой легочной артериальной гипертензией (III подгруппа больных) в раннем послеоперационном периоде в отличие от пациентов с умеренной легочной гипертензией наблюдалось достоверное увеличение объема полости левого желудочка (табл.). Так, КДО сократился с 102,1±10,2 мл до 65,0±14,4 мл (p<0,05), а КСО соответственно с 39,8±6,2 мл до 22,5±4,1 мл (p<0,05). В III подгруппе большинство составляли больные с ДМЖП и ОАП. Известно, что при данных пороках сердца большая нагрузка приходится на левые отделы сердца, поэтому после хирургической коррекции порока объемная нагрузка на левый желудочек сердца
уменьшается. Насосная функция левого желудочка через 1 месяц после операции не изменилась, а показатели сократительной функции по данным фазового анализа систолы левого желудочка сердца имели тенденцию к снижению. Отношение РЕР/ЕТ и РЕР/АТ возросло и составило соответственно 0,51±0,06 и 1,34±0,12 (p>0,05).

В ближайшем послеоперационном периоде у детей с высокой легочной артериальной гипертензией констатировано достоверное снижение давления в полости правого желудочка. Показатели, характеризующие насосную функцию уменьшились, а сократительная способность правого желудочка сердца стала пониженной. Размеры правого желудочка сердца и диаметр легочной артерии оставались на прежнем уровне, возможно, за счет выраженных морфологических изменений со стороны самой мышцы сердца, а также сохранялось достаточное высокое давление в полости правого желудочка сердца, превышающее аналогичное у пациентов I подгруппы в 1,8 раза, а во II – в 1,5 раза.

В отдаленном периоде наблюдения размеры левых камер сердца не отличались от показателей больных сравнимых подгрупп. КДО левого желудочка достоверно увеличился и даже превысил среднее значение здоровых детей (114,5±16,3 мл, p<0,05). При анализе фазовой структуры систолы левого желудочка сердца наблюдалось достоверное увеличение периода изгнания, который вырос до 363,9±14,6 мс (p<0,01), что способствовало повышению сократительной функции миокарда левого желудочка.

Показатели давления в полости правого желудочка сердца и среднее давление в легочной артерии, несмотря на достаточно длительный срок после операции, больше не изменились. Размеры правых отделов сердца несколько сократились, но не достигли показателей в подгруппах детей с умеренной легочной гипертензией. Размер полости правого желудочка сердца индексированный к поверхности тела равнялся 21,6±4,4 мм/м2, что в 1,3 раза превысило значение у пациентов I подгруппы и почти в 2 раза - нормальные величины. Насосная функция правого желудочка сохранялась повышенной. При этом СИ был увеличен и составил 5,8±0,8 л/мин/м2. Показатели сократительной функции в динамике несколько улучшились, но были значительно ниже, чем у детей в группе контроля и с умеренной легочной гипертензией. Так, отношение РЕР/ЕТ у обследованных детей с различной степенью легочной гипертензии составило в I подгруппе 0,31±0,03; во II - 0,45±0,06 и 0,66±0,08 - в III подгруппе.

Заключение

Таким образом, хирургическая коррекция лево-правого шунтирования крови с ассоциированной легочной артериальной гипертензией у детей, существенно меняет центральную гемодинамику, при этом, не оказывая значимого влияния на ремоделирование миокарда а также насосную и сократительную функцию левого желудочка сердца. Тогда как, несмотря на положительную динамику размеров правых отделов сердца, снижение давления в малом круге кровообращения, зависящее от исходной степени легочной артериальной гипертензии, констатировано снижение сократительной функции правого желудочка сердца. Причем восстановление функциональных показателей
сердца и микроциркуляции малого круга кровообращения в отдаленные сроки после выполненной операции в большей степени характерно для больных с умеренной степенью легочной гипертензии.

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