PVRI CHRONICLE

News, Discussions, Science and Medicine from the PVRI

www.pvri.info

8th PVRI Annual World Congress
Guangzhou, China, 2015

Coming together to fight against pulmonary vascular disease
The Journal
PVRI Chronicle (ISSN 2057-5351) is a non-peer reviewed journal published on behalf of the Pulmonary Vascular Research Institute. The journal publishes articles, reviews, and commentaries on the subject of pulmonary vascular diseases and actions within the PVRI. The journal is published biannually online and is available in print on request.

Information for Authors
There are no page charges for submission to the journal. All manuscripts are solicited by the Editorial Board, but submissions may also be made to Executive Editor Nikki Krol at adminpvri@gmail.com.

Subscription Information
Copies are provided to Fellows and members of the PVRI free of charge. PVRI members and Fellows must notify Executive Editor Nikki Krol of a change in their address in order to continue to receive the journal. She can be contacted at adminpvri@gmail.com. PVRI Chronicle is published and distributed by the Pulmonary Vascular Research Institute. Requested print copies are sent to subscribers directly from the publisher’s address. It is illegal to acquire copies from any other source. If a copy is received for personal use as a member of the association/society, one cannot resell or give away the copy for commercial or library use.

Advertising Policies
PVRI Chronicle accepts display and classified advertising. Frequency discounts and special positions are available. Inquiries about advertising should be sent to Nikki Krol at adminpvri@gmail.com.
PVRI Chronicle reserves the right to reject any advertisement considered unsuitable according to the set policies of the journal. The appearance of advertising or product information in the various sections of the journal does not constitute an endorsement or approval of the journal and/or its publisher of the quality or value of said product or of claims made by its manufacturer.

Copyright
The entire contents of the PVRI Chronicle are protected under international copyrights. PVRI Chronicle, however, grants to all users a free, irrevocable, worldwide, perpetual right of access to, and a license to copy, use, distribute, perform and display the work publicly and to make and distribute derivative works in any digital medium for any reasonable non-commercial purpose, subject to proper attribution of authorship and ownership of the rights. The journal also grants the right to make small numbers of printed copies for their personal non-commercial use.

Permissions
To request permission for reproduction of articles or information from this journal, please contact Miss Krol at adminpvri@gmail.com.

Disclaimer
The information and opinions presented in the Journal reflect the views of the authors and not of the Journal and its Editorial Board or the Publisher. Publication does not constitute endorsement by the Journal. Neither the PVRI Chronicle nor its publishers nor anyone else involved in the preparation or the material contained in the PVRI Chronicle represents or warrants that the information contained herein is in every respect accurate or complete, and they are not responsible for any errors or omissions or for the results obtained from such material. Readers are encouraged to confirm the information contained herein with other sources.

Addresses
Editorial Office
Miss N. Krol
Enterprise and Innovation Hub
Giles Lane, Canterbury, Kent
CT2 7NJ Canterbury, UK
adminpvri@gmail.com

Published By
Editorial Office
PVRI Chronicle
Enterprise and Innovation Hub
Giles Lane, Canterbury, Kent
CT2 7NJ Canterbury, UK

Published Online
The journal is available in PDF and ebook format on the PVRI website at http://pvri.info/content/pvri-chronicle
# PVRI CHRONICLE

**Volume 2, Issue 1**  
January - June 2015

## 1 Editorial
PVRI World Congress: Coming together to fight pulmonary vascular disease  
*Sachindra Raj Joshi*

## 2 Guest Editorial
Caring for children and young people with pulmonary hypertension  
*Sheila G. Haworth*

## 3 PVRI News and Activities
- 8th PVRI Annual World Congress Scientific Agenda  
- PVRI Young Council Get-Together and ERS Congress 2014 Munich Report  
  *Michael Seimetz, Michiel Alexander de Raaf*

## 4 Journal Club
### Interactive Discussion
Cold-induced pulmonary hypertension: a distinctive pathological entity of the pulmonary circulation?  
*Aleksandar Petrovic, Michael Seimetz, Akylbek Sydykov, Oleg Pak,*  
*Florian Veit, Himal Luitel, Norbert Weissmann, Ralph Theo Schermuly, Djuro Kosanovic*

The two faces of antioxidants in pulmonary vascular disease: Focus on COPD  
*Michael Seimetz, Djuro Kosanovic, Himal Luitel, Ralph Theo Schermuly,*  
*Michiel Alexander de Raaf, Harm Jan Bogaard, Eveline Baumgart-Vogt, Norbert Weissmann, Srikanth Kamati*

## 5 Art Club
### Infography
Obesity-related PAH in rats  
*Micheel Alexander de Raaf, Rebecca Vanderpool*

## 6 Learners’ Corner
### Did you know?
The discovery of the pulmonary circulation: a debate spanning centuries  
*Abdallah Alzoubi*

### Review
The association between obesity and pulmonary hypertension: a tale of two diseases  
*Mamotabo Matshela*

### Commentary
Pulmonary hypertension in the developing world  
*Salina Gairhe, Zeenat Safdar*
6 Learners’ Corner  
Perspective  
Pulmonary vascular research in Nepal: Prospective and challenges  
Himal Luitel, Akylbek Sydykov, Michael Seimetz, Christina Vroom,  
Hossein Ardeschir Ghofrani, Norbert Weissmann,  
Ralph Theo Schermuly, Djuro Kosanovic  

7 Clinical Corner  
Perspective  
Challenges for Greek PH patients in time of crisis  
Joanna Alissandratou  

Case Report  
Potential association with sildenafil administration with third (III) cranial nerve palsy in pulmonary arterial hypertension patient  
Aikaterini Flevari, Iraklis Tsangaris, Stylianos Argentos,  
Dimitrios Konstantonis, Irini Mavrou, Stylianos E. Orfanos, Ioannis Lekakis,  
Apostolos Armaganidis  

Interview  
Interview with a patient suffering from pulmonary arterial hypertension  
Natasha Sommer  

Interview  
Professor Xiansheng Cheng FPVRI, interviewed by Dr Lan Zhao FPVRI  
Lan Zhao, Nikki Krol  

8 PVRI Annual Report  
2014  
PVRI Meetings  
Nikki Krol, Stephanie Barwick  

PVRI Disease & Speciality Task Forces  
Nikki Krol, Stephanie Barwick  

PVRI Regional Task Forces  
Nikki Krol, Stephanie Barwick  

PVRI Publications  
Nikki Krol, Stephanie Barwick  

PVRI Administrative Activities  
Nikki Krol, Stephanie Barwick
PVRI World Congress: Coming together to fight pulmonary vascular disease

“No one can whistle a symphony. It takes a whole orchestra to play it”.

Wise words from Halford Edward Luccock (1885–1961), a prominent professor of Homiletics at Yale’s Divinity School. These words certainly ring true for the mission of the PVRI, as the fight against pulmonary vascular disease (PVD) is overwhelming and impossible with one individual effort. Instead, it will take the communal effort of many pulmonary vascular disease (PVD) professionals. This community includes clinicians, basic scientists, regulatory bodies, pharmaceutical industries and even patients. PVRI is the family of PVD professionals from around the globe, and they come together, hand in hand, to fight against PVD. Their coming together can be witnessed in the steady increase of PVRI membership, which now consists of over 760 fellows from around the globe. Their active participation in the fight against the pulmonary vascular disease grows stronger every day.

In July 2014, this resulted in a collaboration between the PVRI and the US Food and Drug Administration (FDA), which in turn launched the First Annual Drug Discovery and Development Symposium for Pulmonary Hypertension at the National Institute of Health, Bethesda, MD, USA. Global experts on PVD, right heart failure, and clinical trial designs joined members of the pharmaceutical industry and regulatory authorities to discuss and identify the most promising treatments for future development in the field. The PVRI and the FDA were gratified that the goals of the meeting were accomplished and are looking forward to having similar annual event next year in Europe.

In 2014, the PVRI Chronicle was evolved as a natural progression in the PVRI publication initiative following the success of the PVRI Review. From its first issue, we envisioned PVRI Chronicle to be a professional journal dedicated to news, discussions, science and medicine in the field of PVD around the globe. The response to our first volume of issues, published in January and July 2014, was encouraging. We are thankful for the active participation from members of the PVRI Young Council. We are equally appreciative for the feedback and suggestions for improvement from the eminent scholars in the field of PVD, many of which we are incorporating. One of such improvement is replacing section “Patients’ Corner” by “Clinical Corner”. The new “Clinical Corner” section will better represent all the clinical aspects of PVD including patients’ perspectives, clinicians’ perspective, case studies and clinical trials as suggested by Professor Ghazwan Butrous.

This issue includes an interview with eminent scholar Professor Xiansheng Cheng, in which he presents an early history of the clinical and experimental research of pulmonary vascular disease in China. According to Professor Cheng, the structural and/or functional disorders of the whole or local pulmonary circulation in pulmonary vascular disease is a result of primary or secondary pulmonary vascular lesions. Despite tremendous research over the years, we still lack classification of PVDs and Professor Xiansheng Cheng suggests that the PVRI should take a broader view to explore the whole spectrum of pulmonary vascular disorders and establish the classification of PVDs. For the Journal club section, we have selected two interactive discussions covering cold-induced pulmonary hypertension and antioxidants in pulmonary vascular disease. The Learner’s Corner presents a review article on the association between obesity and pulmonary hypertension; a commentary on PH and the developing world; a perspective on pulmonary vascular research in Nepal; and a Did You Know article on the discovery of the pulmonary circulation. The Clinical Corner holds...
a report on challenges for Greek PH patients in time of crisis; a case report on the potential association of sildenafil administration with third (III) cranial nerve palsy in the pulmonary arterial hypertension patient; and an interview with a patient suffering from pulmonary arterial hypertension.

PVD is an outcome of the numerous abnormalities in the intricate network of pulmonary vasculature. Since the discovery of the assortment of diseases that are referred to as pulmonary vascular disorders, several anomalies have been associated with the pathogenesis of pulmonary vascular disease. These include vasoconstriction, thrombosis, fibrosis, inflammation, and endothelial and smooth muscle dysfunction, which are mediated by microRNAs, lipid mediators, reactive oxygen species, progenitors cells and the list goes on and on with one broad pathological outcome - the pulmonary vascular disease. For such complex events in the pathogenesis of PVD, a particular event alone is not adequate for the pathological outcome. Likewise, to resolve the pathology of the PVD, a particular discovery alone is not sufficient. It takes an array of discoveries with honest, robust and careful integration. In that context, the PVRI World Congress is an effort of the Pulmonary Vascular Research Institute to bring together the PVD professionals to present their discoveries, and to encourage discussion and debate towards the fruitful integration of the outcomes to fight pulmonary vascular disease. PVRI Chronicle will play its vital role in sharing news, discussions, science and medicine from the PVRI among the clinicians, basic scientists, regulatory bodies, pharmaceutical industries and even patients.

As we move into our second year of the PVRI publications initiative, we are one step closer to bringing awareness of pulmonary vascular disease and reducing the PVD associated mortality. Most importantly, in the words of Henry Ford, “coming together is a beginning; keeping together is progress; working together is success”, so let us join hand in hand and work together.

Dr. Sachindra Joshi FPVRI
Editor in Chief PVRI Chronicle
Department of Pharmacology
New York Medical College
Valhalla, NY, United States
Email: sachindraraj_joshi@nymc.edu

The PVRI membership, here pictured during the 8th PVRI Annual General Meeting and 7th PVRI Scientific Workshops & Debates, join forces against pulmonary vascular disease.
Caring for children and young people with pulmonary hypertension

Sheila G. Haworth CBE
PVRI President
Great Ormond Street Hospital for Children
London, United Kingdom

Caring for children and young people is always challenging, however experienced the clinician and however limitless the budget. Skillful management demands a prompt, accurate diagnosis, careful explanation of potential therapies, and information about prognosis. Parents and children need reassurance that they will be cared for indefinitely by a team experienced in the management of pulmonary hypertension. When pulmonary hypertension (PH) is a complication of a recognised disease process, such as congenital heart disease or connective tissue disease, then the parents and children are anxious about the new, additional problem. When a child who was previously thought healthy and entirely normal is found to have an incurable disease, the shock is almost intolerable. All children with pulmonary hypertension need specialised care and should only be treated in ‘centres of excellence’.

Some of us are fortunate enough to be able to offer any therapy required, including lung transplantation, but most physicians are not so fortunate. This is why the PVRI International Guidelines for Patient Management need to be modified for use in the developing world. Professors Ghazwan Butrous and Majdy Idrees have worked hard on producing guidelines for the developing world. Each region or country can amend these guidelines to suit their own needs and resources, and distribute the guidelines in their own language.

In managing any patient with PH the diagnostic algorithm is the same, but the diagnosis is frequently more complicated in children than adults. All the causes of pulmonary vascular disease (PVD) found in adults are seen in children, but children have many additional problems. The development or early maturation of the pulmonary vasculature may be abnormal. The child may be syndromic, when the chromosomal abnormality may or may not have a recognised association with PH. To counter these issues, the PVRI Paediatric Task Force, led by Dr Ian Adatia, produced a new Disease Classification of Pulmonary Vascular Disease in Childhood at the Annual Congress in Panama in 2011. In reality, the long list of possibilities is a box-ticking exercise which ensures that the phenotype is accurately and comprehensively described. In addition, it can be a struggle to describe functional capacity in children using the WHO classification. The 6-minute crawl test doesn’t work! Therefore we worked out a more precise but simple classification of functional ability in children by comparing their performance with that expected in a normal child of the same age: the PVRI Panama Functional Classification.

Paediatric trials are intrinsically complicated, since issues of consent and ethics and long term pharmacovigilance are difficult. New therapies are slow to come to the market, whilst medicines are often expensive and do not provide a cure. Nevertheless, we have made a huge amount of progress in the treatment of children during the last fifteen years and we must persist.

By focusing attention on the needs of children with pulmonary vascular disease the PVRI can and should play a significant role in improving the outlook for these patients.

Corresponding author:
Sheila G. Haworth
PVRI President
Great Ormond Street Hospital for Children
London, United Kingdom
Email: sghlb@computalynx.co.uk
Day 1: Thursday, January 15, 2015

08:00-10:45  Physically re-engineering the cardio-pulmonary circulation
Chairs: Marc Pritzker, USA, Co-chair: Thenappan Thenappan, USA

- Compliance, cardiac output and ventriculo-vascular coupling should be the targets of choice, Harm-Jan Bogaard, the Netherlands
- Mechanical devices for adding compliance to the pulmonary circulation, Marc Pritzker, USA
- Intra-cardiac shunting - when and how, Julio Sandoval, Mexico
- Re-synchronizing the right ventricle, Thenappan Thenappan, USA
- Extra-cardiac shunts, Shahin Moledina, UK
- Pulmonary denervation, Shaolaing Chen, China

10:45-11:00  Tea Break

11:00-13:00  Debate: What should our priority be- directly targeting the BMPR-II or novel combination therapy? A debate based on translational science
Chair: Sheila G. Haworth, UK

A debate based on translational science
- We should directly target the BMPR-II: Nicholas Morrell, UK
- We should target novel combination therapy: Lucy Clapp, UK, and Mandy MacLean, UK

13:00-14:00  Lunch Break

14:00-15:35  Taking a Fresh Approach to Clinical Trials
Chairs: Aaron Waxman, USA, and Ardeschir Ghofrani, Germany

- Keynote discussion: Design and direction of clinical trials in orphan diseases, Tom MacDonald, UK

With steadily increasing drug development costs and timelines and the desire to access global patient populations, conducting clinical trials in Asian, South American and African countries has rapidly become an appealing option for many pharmaceutical companies.

- Why Asia offers good opportunities for clinical trials, Kevin Laliberte, USA
- Advantages and challenges of conducting trials across the world, Hassan Movahhed, USA
• The Perspective from India, Parfulla Kerkar, India
• The Pediatric Perspective – a global problem, Ian Adatia, Canada
• The “n of 1” of clinical trial design – is this the ultimate approach? Brad Maron, USA

15:35- 15:50  Tea Break & Poster Viewing

15:50- 17:20  Patient Registries
Chair: Shahin Moledina, UK, and Barbara Cockrill, USA

• Keynote Presentation: The UK National Incident Case PH Registry – Its role and value, Paul Corris, UK

Isolated patients affected by a rare disorder managed by a single physician will not contribute to progress in the understanding of the epidemiology, pathophysiology, natural history and efficacy of treatments for such disorders. When isolated patients are included in large cohorts that are eventually submitted to careful analysis we can greatly improve our knowledge of these conditions. Registries can be powerful tools in improving our understanding of rare diseases. A critical issue for neglected rare diseases is how to best create networks of reference centers with the aim of establishing national and international registries. Do our current registries live up to this lofty goal? What are the difficulties and limitations of current registries?

• Special issues of pediatric registries, Maria Jesus del Cerro, Spain
• The South African experience, Friedrich Thienemann, South Africa
• Developing a registry in South America, Gabriel F. Díaz, Colombia
• PAH registry, China experiences, Jianguo He, China

17:20- 18:20  PVRI Annual General Meeting

19:00  Dinner, with Task Force Meeting

Day 2: Friday, January 16, 2015

08:00- 09:50  Macrophage diversity in inflammation-related pulmonary vascular remodelling
Chair: Roger Johns, USA, and Stylianos Orfanos, Greece

• Keynote Presentation: The many faces of macrophage activation, Limin Zheng, China
• Macrophage and immune cell cross-talk with endothelium and vascular smooth muscle in experimental pulmonary hypertension, Kurt Stenmark, USA
• Inflammation and PAH - a case study, Jane Leopold, USA
• Putting the brakes on macrophages and immune response in pulmonary hypertension, Roger Johns, USA

09:50- 10:20  Tea Break & Poster Viewing

10:20- 12:30  Pulmonary hypertension in women
Chair: Barbara Cockrill, USA, and Zeenat Safdar, USA
• Keynote Presentation: Pregnancy and pulmonary hypertension: presentation of
**the Task Force document**, Barbara Cockrill, USA
- **Sex differences in PAH**, Mandy MacLean, UK
- **Effect of sex hormones and pregnancy on RV function**, Keri Shafer, USA
- **Contraception and termination in pulmonary hypertension**, Ioana Preston, USA
- **Anticoagulation in pregnancy**, Jess Mandell, USA

**12:30- 13:30**  
**Lunch Break**

**13:30- 15:30**  
**Pulmonary hypertension in congenital heart disease**  
Chairs: Rolf Berger, the Netherlands, and Sheila G Haworth, UK

- **Pulmonary vascular function in increased pulmonary blood flow**,  
  Jeff Fineman, USA
- **Can we predict postoperative outcome after shunt closure?**  
  Hiu Lin Gan, China
- **Preoperative assessment and post-operative management**,  
  GuHong, China
- **Why is operability a matter of debate?** Ian Adatia, Canada

**15:30- 16:00**  
**Tea Break & Poster Viewing**

**16:00- 17:30**  
**MicroRNAs and pulmonary hypertension**  
Chairs: Jane Leopold, USA, and Lan Zhao, UK

*MicroRNAs are powerful regulators in a wide variety of diseases, and the possibility of viewing miRNAs as therapeutic entities are now being explored. MiRNAs have a number of important advantages. They are small entities that consist of a known sequence that is often completely conserved among species: attractive features from a drug development standpoint. Are we ready to use them to target the RV or the pulmonary vascular bed?*

- **MicroRNAs in right ventricular hypertrophy and failure: potential pharmacological targets?** Ralph Schermuly, Germany
- **Exploiting the systems-level regulation of pulmonary hypertension by microRNAs for therapeutic benefit**,  
  Stephen Y. Chan, USA
- **Targeting microRNAs to treat BPD: vascular or airway targeting?**  
  Guofei Zhou, USA
- **Targeting microRNAs to treat PAH: Will we ever get there?** Hyung Chun, USA

**17:30- 18:30**  
**Robyn Barst Memorial Lecture**  
*The pediatric sildenafil trial: what have we learned?*  
Dunbar Ivy, USA

**18:30- 19:30**  
**Poster Viewing & Discussion**  
Chairs: Aaron Waxman, USA, and Ghazwan Butrous, UK

**19:30**  
**Dinner**
### Day 3: Saturday, January 17, 2015

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00-8:30</td>
<td>Opening Ceremonies</td>
</tr>
<tr>
<td>8:30-12:00</td>
<td>Joint Meeting of the Chinese Thoracic Society and the PVRI</td>
</tr>
<tr>
<td>8:30-10:00</td>
<td>Advances in our understanding and management of CTEPH</td>
</tr>
<tr>
<td></td>
<td><strong>Chairs:</strong> Nanshan Zhong, China, Chen Wang, China, and Ardeschir Ghofrani, Germany</td>
</tr>
<tr>
<td></td>
<td>- <em>Chronic Thromboembolic Pulmonary Hypertension &amp; pulmonary endoarterectomy</em>, Michael Madani, USA</td>
</tr>
<tr>
<td></td>
<td>- <em>Assessment of RV function using invasive exercise testing in CTEPH</em>, David Systrom, USA</td>
</tr>
<tr>
<td></td>
<td>- <em>15-Lipoxygenase and 15-Hydroxyeicosatetraenoic Acid regulate intravascular thrombosis in pulmonary hypertension</em>, Daling Zhu, China</td>
</tr>
<tr>
<td>11:00-10:30</td>
<td>Tea Break &amp; Poster Viewing</td>
</tr>
<tr>
<td>10:30-12:00</td>
<td>Translational and clinical research of pulmonary vascular diseases</td>
</tr>
<tr>
<td></td>
<td><strong>Chairs:</strong> Xiansheng Cheng, China, Peixin Ran, China, and Lan Zhao, UK</td>
</tr>
<tr>
<td></td>
<td>- <em>Targeting the Notch3 signaling pathway</em>, Patricia Thistlethwaite, USA</td>
</tr>
<tr>
<td></td>
<td>- <em>Treatment strategies of intermediate risk pulmonary embolism: present and future</em>, Chen Wang, China</td>
</tr>
<tr>
<td></td>
<td>- <em>Designing clinical trials for orphan diseases: creative thinking and adaptability are essential</em>, Tom MacDonald, UK</td>
</tr>
<tr>
<td>12:00-13:30</td>
<td>Satellite Symposia &amp; Lunch Break</td>
</tr>
<tr>
<td></td>
<td>1. <em>Astrazeneca Satellite Symposium</em></td>
</tr>
<tr>
<td></td>
<td>2. <em>Actelion Satellite Symposium</em></td>
</tr>
<tr>
<td></td>
<td>Evidence based medicine; Target therapy of pulmonary arterial hypertension</td>
</tr>
<tr>
<td></td>
<td><strong>Chairs:</strong> Chen Wang, China, and Jian Wang, China</td>
</tr>
<tr>
<td></td>
<td>- <em>Management of pulmonary hypertension: State-of-the-Art</em>, Yuanhua Yang, China</td>
</tr>
<tr>
<td></td>
<td>- <em>Bosentan in the treatment of idiopathic arterial hypertension</em>, Hua Yao, China</td>
</tr>
<tr>
<td>13:30-15:00</td>
<td>Pulmonary arterial hypertension: current status and future challenges</td>
</tr>
<tr>
<td></td>
<td><strong>Chairs:</strong> Weixuan Lu, China, Liangxing Wang, China, and Zhaozhong Cheng, China</td>
</tr>
<tr>
<td></td>
<td>- <em>Updated clinical classification and diagnostic algorithm of pulmonary hypertension</em>, Yuanhua Yang, China</td>
</tr>
<tr>
<td></td>
<td>- <em>Updated treatment algorithm of pulmonary arterial hypertension: viewpoint from most recent guidelines</em>, Zhihong Liu, China</td>
</tr>
<tr>
<td></td>
<td>- <em>New target and pathways for pulmonary arterial hypertension</em>, Manxiang Li, China</td>
</tr>
<tr>
<td></td>
<td>- <em>Pulmonary hypertension: patient education and social support</em>, Rong Li, China</td>
</tr>
<tr>
<td></td>
<td>- Oral Presentations</td>
</tr>
<tr>
<td>15:00-15:30</td>
<td>Tea Break &amp; Poster Viewing</td>
</tr>
</tbody>
</table>
15:30-17:00  State-of-the-art, Guidelines and Clinical practices on the diagnosis and management of pulmonary embolism  
Chairs: Zhuan Ma, China, Qi Wu, China, and Yimin Mao, China

- Diagnostic strategies of pulmonary embolism: an updated viewpoint, Zhonghe Zhang, China
- Therapeutic strategies of acute pulmonary embolism based on risk stratifications: update from the 2014 ESC guidelines, Changming Xiong, China
- New anticoagulants: indications, durations and complications, Yongcheng Du, China
- Specific issues in management of pulmonary embolism: pregnancy, cancer and non-thrombotic pulmonary embolism, Baomin Fang, China
- The prophylaxis of VTE in different conditions: acute medical illness and surgical populations, Xiaoying Li, China
- Oral Presentations

17:00-17:40  Sanofi-Aventis Satellite Symposium  
Specific and difficult issues in management of pulmonary embolism:  
Chairs: Chen Wang, China, and Xiao-ying Li, China

- Diagnosis and treatment of refractory pulmonary embolism, Zhengu Zhai, China
- From the mechanism of venous thrombosis to the VTE screening and prevention at VTE high risk population, Jian-long Men, China
- Oral Discussions

18:30  PVRI - CTS Gala Dinner

Day 4: Sunday, January 18, 2015

8:00-10:00  Ancient and modern wisdom in pulmonary vascular diseases  
Chairs: Rongchang Chen, China, Jianguo He, China, and Jason XJ Yuan, USA

- Traditional Chinese medicine and pulmonary hypertension: therapeutic effects of sodium tanshinone IIA sulfonate, Jian Wang, USA
- Compliance and the pulmonary vascular bed in CTEPH, Stefano Ghio, Italy
- Pulmonary vascular disease in China: past, present, and future, Xiansheng Cheng, China
- Are pulmonary vascular abnormalities a driving force in the development of emphysema? Norbert Weissmann, Germany

10:00-10:30  Tea Break & Poster Viewing

10:30-12:00  Hypoxia and the Lung  
Chairs: Ghazwan Butrous, UK, Fei Xiao, China, and Wenju Lu, China

- High altitude and pulmonary hypertension, Rili Ge, China
- High altitude pulmonary hypertension in the highlanders of Tien-shan: therapy based on understanding mechanisms, Almaz Aldashev, Kyrgyzstan
• Circulating collagen biomarkers as indicators of disease severity in pulmonary arterial hypertension, Zeenat Safdar, USA

**12:00- 12:40 Satellite Symposia**

**Remodulin® Satellite Symposium**

**New Hope for severe pulmonary hypertension in China**  
Chairs: Xiansheng Cheng, China, and Yigao Huang, China

- *Interpretation of Remodulin® Global Clinical Trials*, Changming Xiong, China  
- *Case Presentation 1*, Yuanhua Yang, China  
- *Case Presentation 2*, Shengqing Li, China

**12:40-13:30 Lunch Break**

**13:30- 13:45 Pulmonary hypertension in special conditions**  
Chairs: Kejing Ying, China, Aiguo Dai, China, and Zhenguo Zhai, China

- *Management of SLE related pulmonary arterial hypertension: Recent progress and guidelines in China*, Xiaofeng Zeng, China  
- *Lung transplantation in pulmonary arterial hypertension: indications and evaluations*, Jingyu Chen, China  
- *COPD related pulmonary hypertension: novel biomarkers and pathways*, Qinghua Hu, China

**14:15- 14:30 Tea Break**

**14:30- 16:30 Tricks in the management of pulmonary vascular diseases: lessons and experiences from clinical practice**  
Chairs: Shuang Liu, China, Jinming Liu, China, Juhong Shi, China, and Xiaomao Xu, China

- *Pulmonary vascular malformation and pulmonary hypertension*, Jinming Liu, China  
- *Filling defect in pulmonary artery: thrombosis, embolism, or sarcoma?*, Wanmu Xie, China  
- *Pulmonary arterial hypertension during pregnancy*, Shuang Liu, China  
- *Interventional therapy of pulmonary artery stenosis caused by sarcoidosis*, Shengqing Li, China  
- *Thrombolysis after cardiac arrest due to acute pulmonary embolism*, Kejing Ying, China  
- *Pulmonary vasculitis*, Min Peng, China  
- *Familial pulmonary arterial hypertension*, Chaosheng Deng, China  
- *Management of arrhythmia in Pulmonary arterial hypertension*, Qun Yi, China

**16:30- 17:30 Closing Ceremony**
This year the Annual Congress of the European Respiratory Society (ERS) took place in the beautiful German city of Munich from 6-10 September 2014. The organization was outstanding, and the ERS congress proved an ideal platform for scientists from all over the world to meet, present and discuss their data and news about lung diseases (Figure 1). There were many quite interesting and informative talks and poster presentations about current and future treatments of pulmonary vascular diseases.

It would be wrong to highlight only a few presentations because of the extraordinary work of all well-known scientists, both young and established, who attended the conference. Nonetheless, a very interesting case report from David Langleben entitled “Can we make change happen for a patient with newly diagnosed PAH?”, should be mentioned which could raise hope for many patients suffering from pulmonary hypertension (PH). Dr. Langleben recently demonstrated that the soluble guanylate cyclase stimulator riociguat (Adempas®), approved for the treatment of PH, was quite effective as monotherapy in a PH patient who could not tolerate phosphodiesterase (PDE)5 inhibitor treatment (Figure 2).

Unfortunately, there was no official PVRI Get-Together and only a small number of Young Council (YC) members could attend the congress, including Stylianos Orfanos (Greece), Michiel de Raaf (The Netherlands) and Michael Seimetz (Germany).
Figure 2: Presentation of beneficial effects of riociguat as treatment for pulmonary hypertension, a case study presented by David Langleben

Figure 3: The famous “Hofbräuhaus” in Munich. A) Entrance, B) view inside the building, C,D) colorful menu and typical huge beer mugs (“Maßkrüge”) filled with Bavarian beers.
The well-organised conference meant an abundance of quality sessions, which left little time for collaboration-focused meetings between the three YC members. However, once in Munich, the well-known “Hofbräuhaus” (Figure 3A,B), a bar representative of Bavarian life with different kinds of beer (Figure 3C,D), “Weißwürsten” (Bavarian veal sausages), “Schweinshaxe” (knuckle of pork) and “Hendl” (chicken), proved a welcome meeting spot for Michiel de Raaf and Michael Seimetz. In conversation, the focus lay on the acknowledgement of activity within the YC. This year, the PVRI has introduced a concept which allows the YC members to earn points for various rewards. The points can be earned by writing for the PVRI Chronicle, editing the journal, contributing to the educational website, and similar such activities, in exchange for rewards that include refunded conference registration and financial assistance for purposes of travel to scientific meetings. During the Munich Young Council ‘Mini Meeting’, it was decided that as awards and grants are relatively rare for young scientists, such events should be added to the list. Further, it was agreed that the points are reviewed on an annual basis rather than a half yearly one, to ensure members have enough time to gather the necessary points.

The ERS offered another opportunity to get in contact with other young scientists – the “Young Scientists Networking Evening”. It was free with food and drinks and took place on Tuesday, 9th September from 17:30 until 20:00. It was a nice 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.

YC members attending the conference were also active as Secretary of Scientific Assemblies (S. Orfanos), chair of a session (Session 21, S. Orfanos: Weaning off mechanical ventilation: between NIV and tracheotomy), and giving oral presentations (Session 315, M. De Raaf: Intact serotonin signaling is not required for the development of severe angioproliferative pulmonary hypertension in rats; Session 378, M. Seimetz: Phosphodiesterase inhibitors as promising therapies for cigarette smoke-induced emphysema and pulmonary hypertension (PH) in mice) to contribute with our data and efforts to the field of lung research (Figure 4). In addition to attending sessions, discussing with young people in front of posters, and meeting collaboration partners, attendees also flocked to the

Figure 4: Oral presentations of PVRI Young Council members at the ERS international conference 2014 in Munich. A) Michiel de Raaf, B) Michael Seimetz.
exhibition halls with stands from pharmaceutical companies and other medicine-related companies, which offered not only free coffee, but also the possibility to get new insights about state-of-the-art techniques, devices and drugs from “real life”, far away from basic science (Figure 5).

In summary, it was a fantastic and informative congress giving young scientists the opportunity to present their data in front of many experts in the field, get in contact with other scientists and experts, and to further their experiences in the field of pulmonary vascular research.

At the end of a day of hard work at the congress, the authors of this article returned to the beer garden of the “Hofbräuhaus” to enjoy and recover in true German fashion (Figure 6).

Corresponding Author
Dr. Michael Seimetz
Justus-Liebig-University Giessen
Excellence Cluster Cardio-Pulmonary System (ECCPS)
Universities of Giessen and Marburg Lung Center (UGMLC)
Member of the German Center for Lung Research (DZL)
Aulweg 130; 35392 Giessen; Germany
E-mail: Michael.Seimetz@innere.med.uni-giessen.de
Prelude

It is well-known fact that humans populated not only the comfortable habitats of our planet, but also the regions with harsh environmental conditions, such as high altitude and geographic locations characterized by extreme temperatures. Although the influence of high altitude on pulmonary circulation has been extensively covered in the past and still is the focus of intense research, the effect of extreme temperatures such as cold on the pulmonary vasculature is insufficiently investigated. Following this line of thinking, it is important to highlight the fact that a large part of the human population is permanently or partially exposed to cold environments, including the Arctic regions, high altitude and during the winter in more temperate climates. Therefore, we would like to mobilize the scientists in the field of pulmonary vascular research to share their valuable views regarding the effects of cold exposure on the pulmonary circulation, with the ultimate aim to identify whether cold-induced pulmonary hypertension (CIPH) is a separate form of pulmonary hypertension (PH) with its own patho-physiological features, characteristics and manifestations.

Over 35 years ago the historical paper from the Grover group described the existence of the CIPH in cattle at moderate altitude. Importantly, the authors noticed that animals more sensitive to high altitude hypoxia had experienced more prominent effects of the cold on the mean pulmonary arterial pressure (PAP). It was clear that there was an interaction between these two extreme environments such as cold and high altitude in affecting the pulmonary vasculature, but the underlying mecha-

Cold-induced pulmonary hypertension: a distinctive pathological entity of the pulmonary circulation?

Aleksandar Petrovic¹, Michael Seimetz¹, Akylbek Sydykov¹, Oleg Pak¹, Florian Veit¹, Himal Luitel¹, Norbert Weissmann¹, Ralph Theo Schermuly¹, Djuro Kosanovic¹

¹Universities of Giessen and Marburg Lung Center (UGMLC); Member of the German Center for Lung Research (DZL), Giessen, Germany

Figure 1: Hypoxia and non-hypoxia driven development of the cold-induced pulmonary hypertension. Original photograph: Masan Minic.
nisms remained enigmatic, despite the suggestion that the hypoxia-driven events might hold the key to further understanding. After some years of scientific silence on this topic, Busch et al revealed interesting findings. They demonstrated that cold exposure at high altitudes increased PAP compared to the control and importantly, the oxygen supplementation just partially reduced PAP values, indicating the existence of two possible mechanisms responsible for the CIPH development: hypoxia (due to cold-induced alveolar hypoventilation) and non-hypoxia driven (Figure 1). The following years, Japanese researchers confirmed the acute and semi-chronic detrimental effects of a cold environment on the pulmonary arterial pressure in the rat model. However, profound and comprehensive investigation was still missing. Recently, two published works from the same research group finally provided a detailed description of chronic CIPH characteristics in the rat model and unraveled some of the potential molecular mechanisms (Figure 2). Chronic cold exposure of rats resulted in their development of the classical PH pathological features/manifestations, such as increased right ventricular systolic pressure (RVSP) and right heart hypertrophy, and pulmonary vascular remodeling process.

Systematic investigation discovered that CIPH was associated with augmented inflammation (macrophage (CD68) accumulation), increased nicotinamide adenine dinucleotide phosphate

![Figure 2: Potential and hypothetical pathological mechanisms involved in development of cold-induced pulmonary hypertension.](image)

---

**Figure 2:** Potential and hypothetical pathological mechanisms involved in development of cold-induced pulmonary hypertension. Different signaling pathways suggested to play a role in cold-induced pulmonary hypertension and their interplay are schematically presented (Based on the following literature sources: Crosswhite and Sun 2013, Crosswhite et al 2014, and Li et al 2010). PDE: phosphodiesterase; CD68: cluster of differentiation 68; cGMP/GMP: cyclic guanosine monophosphate/guanosine monophosphate; cAMP/AMP: cyclic adenosine monophosphate/adenosine monophosphate; NADPH: nicotinamide adenine dinucleotide phosphate; ROS: reactive oxygen species; PDGF: platelet-derived growth factor; TNF-α: tumor necrosis factor alpha; IL-6: interleukin-6; PH: pulmonary hypertension. Original photograph: Masan Minic.
(NADPH) oxidase activity and reactive oxygen species (ROS) production, upregulation of phosphodiesterase (PDE)-1C, and the potential interplay between different signaling pathways (Figure 2). In addition, PDE-1 inhibition led to significant reduction of the CIPH, suggesting the future potential therapeutic candidate.9

Further following this line of thinking, we would like to indicate the fact that these pathological signals and events, such as inflammation, PDEs, NADPH oxidase and ROS are already known players in the PH field. In the next publication the authors found that two inflammatory cytokines, such as tumor necrosis factor (TNF)-α and interleukin (IL)-6 were also augmented in the lungs and/or pulmonary arteries, unraveling further the complex inflammatory axis in the CIPH. Importantly, the inhibition of the TNF-α resulted in CIPH attenuation with reduction of the TNF-α, IL-6 and PDE-1C expression and decrease of lung inflammation, suggesting another potential therapeutic candidate and confirming the inflammatory phenotype of the CIPH pathology (Figure 2). It is worth mentioning that both inflammatory cytokines (TNF-α and IL-6) are well-known in the PH context.16, 17

We would further like to suggest the possibility that platelet-derived growth factor (PDGF) signaling may be involved in the pathological game, as shown in the broilers model of the cold-induced pulmonary vascular remodeling.18,19

Giesbrecht summarized the effects of the cold exposure on the respiratory system covering also the pulmonary circulation, and indicated that there were some interesting data in the Russian literature describing the existence of the CIPH in humans. Almost 40 years ago, Milovanov published an article showing that the post mortem morphology of the pulmonary vessels in the healthy men from Magadan (Northeastern region of Russia) revealed the presence of the “hypermuscularization of arteries”. Later it was found that the natives from the cold climates of the Northeast Russia had augmented values of the systolic PAP and some indigenous groups had clear signs of right ventricular hypertrophy.20.21.23 According to Milovanov et al these above mentioned phenomena were defined as the “North pulmonary arterial hypertension” (Северная легочная артериальная гипертензия). Similar to the Russian findings, the investigation of the long-term living residents in extreme temperature environment of the Canadian Arctic provided the description of the age-related abnormalities, such as right heart hypertrophy and some patterns of pulmonary vascular remodeling.

In the end, chronic cold exposure in the rat model resulted in development of moderate PH, relatively similar to the chronic hypoxia-induced PH in mice. Together with the fact that hypoxia-driven mechanisms are part of cold-induced pathological events in the pulmonary circulation and that high altitude hypoxia and extremely low temperature conditions exert combined effects, we would like to bravely suggest that the CIPH is a separate entity which may be included in the clinical classification of the PH, probably in the group 3.

THE QUESTION FOR INTERACTIVE DISCUSSION

We would like to suggest the following question to the scientific community worldwide: Is cold-induced pulmonary hypertension indeed a distinctive pathological entity of the pulmonary circulation in a given extreme environment? All experts and others interested in this field are welcome to reply and express their point of view and perspectives on this topic, in the next volume of PVRI Chronicle.

References

cold temperature and its association with pulmonary hypertension in broilers with pulmonary hypertension induced by -


Eiseigaku Zasshi 48:859-863.


Prelude
Based on a variety of scientific reports, but also on sales promotion, antioxidants became quite popular dietary supplements. People thought and still believe antioxidants would reduce disease, boost system performance and perhaps even slow the aging clock. But the reality is not quite so glorious. It is true that in some cases, high amounts of antioxidants are helpful. However, in other cases they can be harmful. It is only a slight exaggeration to say that for every study that shows benefits, there is another study that does not. In terms of diseases associated with oxidative stress, such as chronic obstructive pulmonary disease (COPD), antioxidant supplementation may make sense. Yet even so, some studies showed beneficial effects on the health of COPD patients, and other studies demonstrated that there was no difference between antioxidant-treated and placebo-treated patients. Thus, there is a controversy which will be discussed in this article. This interactive discussion aims to challenge scientists and other persons who are interested in this field to express their views about the usefulness of antioxidant supplementation for the treatment of pulmonary diseases associated with, but also independent of oxidative stress.

Oxidants and oxidative/carbonyl stress
Based on the anatomy (high blood supply and large surface area) and physiological role of the lungs, they are permanently exposed to high oxygen levels. Furthermore, the lung epithelium is constantly exposed to endogenous oxidants produced during mitochondrial respiration and by activated inflammatory cells. But also exogenous sources of oxidants such as cigarette smoke and air pollutants, e.g. ozone, combustion particles and nitrogen dioxide, affect the lung epithelium. Under normal conditions there is a balance of oxidants and antioxidants to ensure critical amounts of oxidants do not occur. Under pathological conditions, such as COPD, there is an oxidant/antioxidant imbalance in favor to oxidants resulting in oxidative and subsequent carbonyl stress. Oxidative stress is mediated by reactive oxygen species (ROS), either nonradical (hydrogen peroxide) or oxygen radicals (superoxide, hydroxyl radical). The unstable radicals with unpaired electrons can initiate oxidations themselves, or together with reactive nitrogen species, they can cause a couple of harmful effects such as apoptosis, cell necrosis, senescence, autophagy, inflammation, epigenetic changes, remodeling of extracellular matrix and blood vessels, endothelial dysfunction, inactivation of antiproteases, mucus hypersecretion, worsened tissue repair, lipid peroxidation and protein carbonylation (Figure 1). Carbonyl stress, a consequence of oxidase stress and the accumulation of carbonylated proteins whose functions are altered, is increasingly recognized as a major driver for chronic diseases.

Michael Seimetz¹, Djuro Kosanovic¹, Himal Luitel¹, Ralph Theo Schermuly¹, Michiel Alexander de Raaf³, Harm Jan Bogaard³, Evelyne Baumgart-Vogt², Norbert Weissmann¹, Srikanth Karnati²

¹Excellence Cluster Cardio-Pulmonary System (ECCPS), Universities of Giessen and Marburg Lung Center (UGMLC), Member of the German Center for Lung Research (DZL), Giessen, Germany
²Institute for Anatomy and Cell Biology II, Division of Medical Cell Biology, Justus Liebig University, Giessen, Germany
³Department of Pulmonology, Pulmonary Arterial Hypertension Knowledge Centre, VU University Medical Center, Amsterdam, The Netherlands
and is present in both smokers and COPD patients.6,7

Excessive amounts of oxidants can lead to oxidation of essential molecules in the organism. For instance, molecules of the vasculature that form the walls of arteries, become oxidized when they lose an electron. Once oxidized, they become unstable and easily break apart. Moreover, oxidative stress can result in enhanced inflammatory gene expression, failure to resolve the inflammatory response, corticosteroid insensitivity, a decreased capacity to induce endogenous antioxidant defenses, and a rapidly aging lung in COPD with increased risk of developing emphysema.3 However, not all free radicals are bad. In fact, free radicals are necessary for life. For instance, the organism cannot turn air and food into chemical energy without a chain reaction of free radicals. Free radicals are a natural byproduct of breathing. They are also a crucial part of the immune system by attacking foreign invaders, such as bacteria. They can also act as second messengers and thereby play an important role in signal transduction.3,8

**Antioxidants as dietary supplements**
Antioxidants have the ability to neutralize oxidants and protect the body against oxidative stress. Some of the most common antioxidants are the vitamins C and E, selenium and beta carotene. Over the last two decades, a number of studies have suggested that COPD risk is
associated with diets lacking in vitamins and antioxidants. Low diet-intake of vitamins has been reported to reduce natural defenses and increase the probability of airway inflammation. Furthermore, a high intake of fruits and vegetables has been associated with a lower risk of COPD, lower mortality and an improvement of spirometric values. A profound systematic review by Tsiligianni and van der Molen revealed that a variety of studies and reviews highlight an association of vitamins with lung function in healthy subjects and COPD patients and a reduction in symptoms, respiratory infections and exacerbations. Moreover, it is suggested that an increased vitamin intake may reduce the annual decline of FEV1 (forced expiratory volume in 1 second). However, there was no clear evidence of the benefit of vitamin supplements. Most studies regarding supplements showed no benefit of multivitamin supplementation in symptoms, spirometric function or hospitalization for COPD.

The epithelial lining fluid, which protects the surface of the lung from the environment, contains several antioxidants including ascorbic acid (vitamin C), α-tocopherol (vitamin E), and uric acid. Several studies have shown a clear association between reduced levels of vitamin C and E and worsened pulmonary function in COPD. However, this may simply reflect an increased oxidative burden as a result of repeated exacerbations. To date, there are no studies clearly showing that dietary supplementation with antioxidants can lead to clinical improvement. However, a 10-year follow-up study did find that antioxidant supplementation reduced the risk of of the development of chronic lung disease by 10% and lowered carbonyl stress levels in the lung. Although there initially was enthusiasm for the use antioxidants for prevention of disease and improvement of health, over the years neutral and even negative reports surfaced about the benefits of antioxidant supplements. As an example, in 1994, a study published in the New England Journal of Medicine reported that there was no reduction in the incidence of lung cancer among Finnish male smokers after five to eight years of dietary supplementation with vitamin E or beta carotene. In contrast, the smokers receiving a beta carotene supplement were 18 percent more likely to develop lung cancer.

The explanations why antioxidant supplementation does not work satisfactorily in most of the patients suffering from oxidative stress-related diseases are manifold and remain in part speculative. One important issue seems to be the role of ROS in signal transduction and immune response which may be abolished by high doses of antioxidants. Moreover, the term ‘antioxidant paradox’ should be mentioned. It is “often used to refer to the observation that oxygen radicals and other ROS are implicated in several human diseases, but giving large doses of dietary antioxidants to human subjects has, in most studies, had little or no preventative or therapeutic effect”. The author Barry Halliwell, a pioneer in the field of free radicals and antioxidants, has some interesting explanations regarding his introduction of the term ‘antioxidant paradox’. He suggests that high amounts of antioxidants might be turning into pro-oxidants, fueling free-radical production and its damage. This theory is supported by findings from Carr and Frei. However, low levels of pro-oxidants can be good, exerting a mild stressful challenge that triggers a rapid response, leading to increased levels of endogenous antioxidant defense systems. This dose-dependency of pro-oxidants is consistent with Paracelsus’ popular sentence: Dosis facit venenum - The dose makes the poison. Furthermore, the time point of application can also be critical. Vitamin C can worsen cell damage once it has already started. Several studies have shown that people who did not get the daily recommended allowance of vitamin C had an increase in free-radical damage to their DNA. But, paradoxically, people who took megadoses of vitamin C also had an increase in DNA damage.

Halliwell argues that a varied diet seems to be healthier than simple supplement-taking because the isolated antioxidant might not be sufficient. Fruits and vegetables are rich in antioxidants and contain hundreds of other chemicals. It is unlikely that any single chemical or combination of chemicals might pack the therapeutic punch.
Finally, according to Halliwell, to minimize oxidative damage, one should eat well including plenty of fruits, grains and vegetables, avoid obesity, not smoke and exercise regularly (also a mild pro-oxidant challenge that triggers beneficial adaptation).  

**The question for interactive discussion**

Based on the existing controversies regarding the beneficial effects of antioxidant supplementation, we would like to postulate the question: Should antioxidant supplements be used in oxidative stress-related pulmonary diseases or is it just a waste of money, effort or even harmful? We invite all experts and persons/scientists interested in this field to reply and express their valuable views on this important scientific and clinical issue, in the next volume of PVRI Chronicle.

**References**


**Corresponding Author**

Dr. Michael Seimetz
Justus-Liebig-University Giessen
Excellence Cluster Cardio-Pulmonary System (ECCPS)
Universities of Giessen & Marburg Lung Center (UGMLC)
Member of the German Center for Lung Research (DZL)
Aulweg 130; 35392 Giessen; Germany
E-mail: Michael.Seimetz@innere.med.uni-giessen.de
**Infography**

**Obesity-related PAH in rats**

Michiel A. de Raaf¹, Rebecca Vanderpool²

1. University of Amsterdam, Amsterdam, the Netherlands
2. University of Pittsburgh Medical Center Pittsburgh, United States

**Motivation**

- Obesity has been linked to a number of comorbidities.
- Pulmonary hypertension is thought to be linked to obesity through hyperventilation and hypoxia.
- Role of metabolic and inflammatory disturbances in PH is not fully characterized.

**Questions**

Does pulmonary hypertension develop in obese rats in the absence of hypoxia?

What role do metabolic and inflammatory disturbances play?

**Results**

Klemm et al. Pulm Circ. 2014

Obesity-related pulmonary arterial hypertension in rats correlates with increased circulating inflammatory cytokines and lipids, and oxidant damage in the arterial wall, but not with hypoxia.

- Diet resistant rat strain
- Diet induced obesity rat strain

10kcal% fat, 60kcal% fat

5 months

no PH, PH, PH, PH

smooth muscle cell hypertrophy, more actin-positive arterioles

This study suggests that the genetic/metabolic environment alone can also elicit changes in pulmonary hemodynamics.
Did You Know...

... that the credit for the discovery of the pulmonary circulation is still a topic of debate amongst scientists and historians alike? This argument revolves around whether individual contributions were made independently of one another. Here, we offer the reader a fictitious scene to portray such controversy; the main characters being five legendary names accredited for the discovery of the “lesser circulation” (Figure 1). Excerpts from their original textbooks are italicized for easier referencing. The plot of the scene is adapted from the famous dialectics written by the Greek philosopher Plato; his masterpiece “Apology” in particular, with Plato himself portrayed as the judge between the conflicting scientists.

Scene

It is sometime past midnight... So faint is the rhythmic ticking of the clock, as it has been largely masked by the incomprehensible noises of a group of men congregated by a round table. Mumbling is the only audible sound, and as such, the discussion seems to be going nowhere. Plato’s task is to bring discipline back to the table.

PLATO (angrily):
“Order, order, O scientists! At my time of life I ought not to be appearing before you, in the character of a juvenile judge, let no one expect it of me! However, at your request, from me you shall hear the whole truth, and nothing but the truth, however, delivered after your manner, in a set oration duly ornamented with your own words and phrases! Now, out of your heated arguments earlier, I could understand that the first recorded mention of the circulation is ascribed to Dr. Galen. However, then, the stage is his to start.”

GALEN (full of pride and majesty):
“Your Honor, gentlemen; I suggested that the liver manufactures the natural spirits (blood), and is accordingly the origin of all veins. On the other hand, the heart is the generator of vital spirits and of heat, in addition to being a chief cistern of the blood. In the heart, the thinnest portion of the blood is drawn from the right ventricle into the left, owing to there being perforation in the septum between them: these can be seen for a great part (of their length); they are like a kind of fossae with wide mouths, and they get constantly narrower; it is not possible, however, actually to observe their extreme terminations.”

A constant humming suddenly breaks into the room!

SERVETUS (whispering): “And here begins the fun!”

HARVEY (screaming emphatically):
“But, by Hercules, no such pores can be demonstrated, nor in fact do any such exist!”

GALEN (emphatic in his response):
“I can assure you nothing is done by nature in vain, nature has overlooked nothing! And as I
observed, the insertion of the vena cava into the heart is larger than the vein which is inserted into the lungs. This suggests that not all the blood given to the heart is driven away again into the lungs, but rather shunted directly to the left ventricle!”

AL-NAFIS (in his rather deep and tranquil voice):
“Based on my observations, I affirm that there are neither visible, nor invisible, passages between the two cavities, the substance of the heart there being impermeable. The pores of the heart there are compact and the substance of the heart is absolutely thick.”

VESALIUS (jumping to the defense of Galen):
“Calm down, people! Truthfully, Dr. Galen, I also couldn't find these holes, and I dared to admit it publicly, for which I was (he grimaces in disgust)) undeservedly ostracized from Padua’s scientific community! This being said, I would…”

SERVETUS (interjecting loudly, and quite awkwardly):
“Oh good God! Ostracized? You think this is bad? Son: me, and all copies of my book, Christianismi Restitutio, were burnt at the stake, punished by the Holy Inquisition, for rejecting Trinity in the Bible! And, believe you me, it still hurts!”

Uncomfortable amusement encompasses the room. Plato, however, orders Vesalius to finish his part.

VESALIUS
“I was saying: I would attribute Galen’s shortcomings to the fact that he carried out his dissections on primates, mainly Barbary Apes, and not on human cadavers, since the latter had been banned in ancient Rome.”

PLATO: “Fair enough! May you continue Dr. Galen.”

GALEN (unmoved by the huge opposition so far):
“The blood flow through the lungs is unidirectional, I noticed. Part of the blood in the right ventricle passes through the arterial vein (pulmonary artery) to nourish the lungs. The venous artery (pulmonary vein), on the other hand, carries air from the lungs into the left ventricle to mix with blood, and a portion of the spirituous blood moves on the opposite direction for lungs’ refreshment, while fuliginous vapors from the heart escape by it into the lungs.”

((Poor Galen!)), one has to think, with the...
group’s impetuous burst of noises! Recognizing his part here is over; he takes a step back and gives his aging body a rest.

SERVETUS (contemplating a golden opportunity to stamp his legacy on the subject, expresses boastfully):

“Well, Your Lordship, I think I’m the first to criticize this Galenic doctrine on the lesser circulation! An extract from my book reads: the subtle blood is transferred from the right ventricle, in a brilliant way, by following a long circuit through the lungs, which submits it into a transformation, in order for the blood to come out colored yellow: the arterial vein transports it into the venous artery. From that moment on, the blood is mixed in that very same venous artery with the inhaled air in order to become re-purified from all fuliginous materials. In this way, the entirety of this mixture is finally attracted by the left ventricle of the heart, during the diastole, to serve as a base for the vital spirit.”

AL-NAFIS (clearly stunned!):

“My friend, when did you publish your book?”

SERVETUS: “Back in 1553.”

AL-NAFIS (indignantly):

“Then, by the Grace of Almighty Allah, how were you the first to condemn Galen’s hypothesis on the pulmonary circulation, when I already did the same almost 300 years before, in 1242! I explained in my Commentary on the Anatomy of Avicenna’s Canon that when the blood has become thin in the right ventricle, it is passed into the arterial vein to the lung, in order to be dispersed inside the substance of the lung, and to mix with the air. The finest parts of the blood are then strained, passing into the venous artery reaching the left of the two cavities of the heart, after mixing with the air and becoming fit for the generation of pneuma.”

More murmurs from the crowd....

HARVEY (astonished):

“Oh dear Lord; what you mentioned earlier, Servetus, sounds like a faithful translation of what Al-Nafis has just explained!”

SERVETUS (arrogantly):

“I cannot be more oblivious of such information, I have to say!”

Though tempted by this new piece of evidence from Al-Nafis, PLATO opts to dig deeper for further clarification.

“I think, gentlemen, there is still a missing link here, as Servetus’ active career was mainly in Spain, France, and Italy, while Al-Nafis resided for the most part of his life in Damascus. We should never overlook the broad cultural, geographical, and language borders between the two! This is most critical to settle the issue of whether the Latin West had access to Al-Nafis’ writings, I believe.”

ALPAGO, who had been silent thus far, decides to intervene:

“Your Honor, my fellows; I lived in the Middle East, mainly Damascus, for almost 30 years; collecting, translating and editing the works of Arab physicians. On my return to Venice in 1547, I published my Latin translations of several parts of Al-Nafis’ Commentary. I also passed much of my acquired expertise orally or in writings hitherto unpublished to my colleagues in Italy. A sudden burst of activity in the fields of anatomy and physiology happened then after at Padua, which ultimately culminated in Harvey’s great book (De Motu Cordis) published in 1628! Having said that, I don’t strive to take from these great investigators any honor that is their due!”

HARVEY: “No objection, Dr. Alpago! I have always genuinely ascertained that true philosophers, who are only eager for truth and knowledge, never regard themselves as already so thoroughly informed, but that they welcome further information from whomsoever and from wheresoever it may come. I explicitly ratify that my biggest en-
deavor was to develop a dynamic total concept of the cardiovascular system as opposed to the anatomical descriptions of separate individual structures that had been available up to my time. It was always my conscience that what is true may be confirmed, and what is false set right by dissections, multiplied experience, and accurate observations!"

This is the light at the end of the tunnel! A few simple words of wisdom may dissipate all the residual heat of an argument, and signs of contentment are forced back onto the faces of the group.

PLATO (concluding the case): "My friends: so persuasively did each of you speak, that a juvenile judge like me may stumble in his noble pursuit of justice! But, then, why bother making judgments when the collective virtue of a case is conceivably worthier than the minute gains of personal glory! Though scientific discoveries are true portraits of the acts of genius, inspiration, and persistence; they are seldom born on air. Pieces of knowledge are thrown all over the streets waiting for an enlightened person to collect and utilize!

Dear all: Thank you! We are most grateful for releasing our minds from the flames of sand and the potency of sky in the barren deserts of ignorance and illiteracy!"

[THE STAGE GOES DARK, AS OUR MINDS ARE ILLUMINATED]

REFERENCES:

Corresponding author:
Abdallah Alzoubi, MD, PhD
Center for Lung Biology,
University of South Alabama,
Mobile, AL, 36688, USA
E-mail: aaa704@jagmail.southalabama.edu
The association between obesity and pulmonary hypertension: a tale of two diseases

INTRODUCTION
Obesity is a complex metabolic disorder often associated with multiple systemic and cardiovascular diseases which contribute to increased morbidity and mortality. Although the relationship between obesity and systemic hypertension has been well reported, its relationship with pulmonary hypertension (PH) is only emerging. However, as there are still some conflicting reports regarding the association between PH and obesity, it is worth reviewing the interaction between the two. Indubitably, the prevalence of obesity in the USA has increased substantially in the last 10 years, yet this seems to have leveled off between the years 2003 and 2010.1-3 The purpose of this paper is to briefly discuss the association between obesity and pulmonary hypertension, postulated pathological mechanisms linking obesity with PH, and general evaluation and treatment of PH in obesity.

PULMONARY HYPERTENSION
Pulmonary hypertension is defined by a mean pulmonary artery pressure of at least 25mmHg at rest or 30mmHg with exertion based on right heart catheterization. PH is classified according to the Dana Point classification, which was developed at the 4th WHO world symposium in 2008. This classification constitutes of five different groups, as follows: Group I is mainly pulmonary arterial hypertension (PAH), and this group responds well to specific pulmonary vascular remodeling agents; Group II is pulmonary hypertension due to left heart disease; Group III is PH to lung diseases or chronic hypoxia; Group IV is chronic thromboembolic pulmonary hypertension (CTEPH); and Group V focuses on pulmonary hypertension related to unclear multifactorial mechanisms. Extensive discussion of this classification will not be covered in this short review paper.

COEXISTENCE OF OBESITY AND PULMONARY HYPERTENSION
Even though data are still limited on the prevalence of pulmonary hypertension as the consequence of obesity, the relationship between obesity and right ventricular dysfunction is reported as a result of pulmonary hypertension. There are multiple postulated mechanisms linking manifestations of obesity in some patients. However, it is vital to consider other potential etiologies of PH in these patients, as obesity is commonly associated with co-morbidities which could potentially be the primary case of pulmonary hypertension.

MECHANISMS OF PULMONARY HYPERTENSION
Due to the complexity of obesity, its impact is related to the structural changes in the pulmonary vascular system. However, some reports have documented immune and vascular cell accumulation within pulmonary arterial lumen, which is believed to be the most important mechanism in all types of pulmonary hypertension.

1. Adiponectin deficiency: With regard to pulmonary arterial hypertension (PAH), PH is thought to be as the result of an imbalance between vasodilator and vasoconstrictor markers in the pulmonary vessels. Adiponectin has direct vasodilator activity and its deficiency is
associated with impairment of vasodilatation which involves the pulmonary vessels, and
the development of systemic hypertension.4-7 Currently there are more data strongly dem-
onstrating an association between adiponectin deficiency and impaired vasoactivity.4,8

2. Obesity associated hypoventilation syn-
drome: Obesity hypoventilation syndrome (OHS) occurs commonly in patients with at
least moderate obesity, BMI > 35kg/m2 and is very rare in those with mild obesity.9 OHS
associated mediators for pulmonary hyperten-
sion include diurnal hypoxemia, hypercapnia and acidosis; however, in severe obesity sec-
ondary contributors are found, which include restrictive lung disease related to the severi-
ty of obesity, and thoracic pressure changes during the respiratory cycle due to increased
upper airway resistance. Obesity hypoventil-
ation syndrome-induced chronic hypoxemia leads to pulmonary arterial remodeling, and
over a period of time the pulmonary arterial hypertension changes from vasoconstriction
to one of endothelial dysfunction, arterial
call wall thickening and fibrosis.10 Previous small
studies demonstrated that OHS is commonly
associated with more severe pulmonary hyper-
tension than in patients with obstructive sleep
apnea.11

3. Obstructive sleep apnea (OSA): OSA is a
well-recognized cause of PH and characterized
by recurrent obstructive episodes and daytime
somnolence. Postulated pathophysiological
mechanisms of pulmonary hypertension in
OSA are related to repeated episodes of noc-
turnal hypoxemia, hypercapnia, acidosis, symp-
pathetic hyperactivity and changes in thoracic
pressure. All these episodes lead to pulmonary
arterial vasoconstriction with subsequent pul-
monary arteriolar remodeling.12

4. Drugs and toxins: Anorexigen has been
associated with the development of pulmonary
hypertension which is likely not reversible after
discontinuing the drug. It was first reported
in 1996, when the use of methamphetamine
analogues were discontinued following a six-
fold increase in the risk of pulmonary hyper-
tension.10,13 Aside from PH, these analogues
were also linked to the development of cardiac
valvular pathologies and cardiac fibrosis. These
drugs, particularly fenfluramine and dexfen-
fluramine, inhibit a specific potassium channel
and inhibition of the current lead to opening of
an L-type calcium channel which is associated
with pulmonary arterioles vasoconstriction.10,14
Most importantly, aminorex are also linked
with an excessive release of serotonin precu-
sors from platelets, and these precursors are as-
associated with pulmonary vasoconstriction and
mediation of smooth muscle proliferation.

5. Obesity associated myocardial dysfunction: Obesity, and particularly morbid obesity, is
linked to heart failure and current reports
indicate a two-fold increase of congestive heart
failure in obese patients. Severe obesity is
commonly associated with diastolic dysfunc-
tion or diastolic heart failure. This generally
leads to elevated left ventricular filling pres-
sures with left heart failure syndrome, which
consequently may increase pulmonary venous
pressure, pulmonary arteriolar remodeling and
fixed pulmonary vascular resistance over time.
Obesity-associated pulmonary hypertension
secondary to myocardial dysfunction could be
explained on the basis of myocardial steatosis,
which bears some similarities to hepatic ste-
atosis and could also be ascribed to excessive
left ventricular (LV) volume load in severe
obesity.10 It is very important to address other
associated contributors which could explain
LV myocardial dysfunction in obese patients
i.e. insulin resistance, sympathetic tone over-
activity, renin-angiotensin system activity and
pre-existing endothelial dysfunction from
other potential etiologies.10,15

6. Chronic thromboembolic disease: There
are multiple postulated prothrombotic mecha-
nisms which are linked to the occurrence of
pulmonary hypertension in obesity. There is
a strong literature link between obesity and
insulin resistance with thrombotic and throm-
bo-embolic phenomenon, and these include
deep venous thrombosis and pulmonary em-
bolism.16-18 In addition, a sedentary lifestyle,
chronic low grade inflammation and OSA are
well recognized risk factors and are linked to
obesity and venous thromb.
7. Associated metabolic disorders: endothelial dysfunction is a well-known link in the development of pulmonary hypertension in a handful of pathological states. Insulin resistance is one important mechanism and should be attended to, as the treatment of insulin resistance with insulin sensitizing drugs does reverse pulmonary hypertension in obese patients.10,22,23 Hyperuricemia is also associated with endothelial dysfunction, and an important pathological mediator of PH.24,25

**Management**

The general approach to the evaluation of PH in obese patients bears no differences to non-obese patients. Both groups will have their full medical history taken, and together with a clinical examination, this forms the crucial basis for pulmonary hypertension evaluation in these patients. A careful diagnostic approach should be applied and this includes biochemical tests, imaging modalities and invasive measures. Although echocardiography is a useful tool with reasonable sensitivity and specificity for the estimation of pulmonary arterial pressure, right heart catheterization remains the gold standard.26 Additional tests may be warranted, although the decision will be guided by findings from the initial investigations, and will subsequently help guide further treatment.

**Treatment**

Pulmonary hypertension in obese patients should be managed with great caution. Weight reduction by different approaches has shown to be quite beneficial in reducing pulmonary arterial pressures and improving the functional capacity in these patients. Similarly, weight reduction by lifestyle modifications and surgical means, particularly in those with morbid obesity, has shown to be beneficial in improving left ventricular diastolic dysfunction.27,28 Therefore, specific therapy directed at additional risk factors and complications have been shown to improve diastolic dysfunction in these patients.

Drug therapies targeting certain areas have shown significant improvement in patients’ symptoms and functional capacities.29 Well studied drugs include phosphodiesterase inhibitors, endothelin receptor antagonists and prostanoids. Intravenous epoprostenol have been shown to reduce mortality in pulmonary hypertension.29 It is important that specific therapies in pulmonary hypertension are directed to additional or other co-morbidities or complications, based on the clinical classification of PH.

**Summary and conclusion**

Obesity is a complex condition associated with cardiovascular complications, of which pulmonary hypertension should be considered in those with dyspnoea. The diagnostic approach for pulmonary hypertension in obese patients is similar to non-obese patients, as transthoracic echocardiography should be considered for the documentation of elevated pulmonary pressures and in assessing the severity and complications of the disease, in order to guide the management of the patient. Weight reduction is the treatment of choice with a variety of means which could be very effective in the managements of these patients. Other treatment modalities should be directed to the causes of pulmonary hypertension and complications thereof.

**References:**
4. Summer R, Walsh K, Medoff BD. Obesity and pulmonary arterial hypertension: Is adiponectin the molecular link between these conditions? Pulm Circ. 2011;1:440-447


Corresponding author:
Dr. Mamotabo R. Matshela, MB, CHB
University of Kwa-Zulu Natal,
Durban, South Africa
E-mail: mamotabomatsh@gmail.com
Pulmonary arterial hypertension (PAH) is considered a rare disease, and is listed on the NIH Office of Rare Diseases Research website (http://rarediseases.info.nih.gov/). While rare, PAH is a devastating disease of the small pulmonary arteries that rapidly leads to right heart failure and premature death. Its exact incidence is unknown but according to British, American, French, and Scottish registries the annual estimated incidence is 2-10 cases per million of population per year. The updated REVEAL registry in 2010 showed poorly understood female predominance with a 4:1 female to male ratio. The estimated median survival of untreated PAH patients is between 2 to 3 years. The disease is insidious, and patients are generally not diagnosed until they begin to experience symptoms of right heart failure.

Most PAH patients are unresponsive to treatment with calcium channel blockers. A recent meta-analysis of 23 randomized controlled trials of three commonly used classes of drugs (prostanoids, endothelin-1 receptor blockers, or phosphodiesterase type-5 inhibitors) shows that while the treatment achieves moderate improvement in symptoms, hemodynamics, and survival, the patient morbidity and mortality rate remain unacceptably high. At present, lung transplantation is the only potential cure of PAH. However, these studies are performed mostly in developed countries. The clinical and pathological course of PAH in developing countries is still poorly understood and considered non-existent. In a recent paper by Idrees et al, the authors succinctly demonstrated clinical characteristics of PAH based on a single center experience in Saudi Arabia.

PAH is a spectrum of diseases, a group of disorders characterized by drastic elevations of the pulmonary arterial pressure leading to right heart failure and death. Most interesting of all are pathologic features that are common to all PAH patients regardless of the presence or absence of associated conditions. The lack of definitive studies in the developing world makes it impossible to estimate the true burden of pulmonary hypertension and this study is a step forward in the fight against PAH.

Although a breakthrough in the field of pulmonary hypertension came along with cardiac catheterization in 1944, developing countries still only have very limited and rare access to this important procedure for diagnosis. In absence of hemodynamic parameters, the diagnosis of pulmonary hypertension is established via conventional clinical methodology. A compatible clinical picture (e.g. dyspnea with exertion, palpitation, chest pains, cyanosis), with signs of cardiomegaly on a chest radiograph, and right axis deviation and/or right ventricular hypertrophy on an electrocardiogram are all supportive of the diagnosis, although misdiagnosis is more common. Therefore, the inclusion of hemodynamic parameters by Idrees et al increases the strength of their study.

This study highlights the demographic differences in PAH in different continents and suggests that PAH occurred earlier than previously assumed in Saudi Arabia. Additionally, the mean age of the PAH patient in this study was relatively younger than what had been previously established as the mean age of 31

Learners’ Corner

Commentary

Pulmonary hypertension in the developing world

Salina Gairhe, Zeenat Safdar

1Division of Pulmonary, Critical Care, Clinical Center, National Institute of Health, Bethesda, MD, USA
2Division of Pulmonary, Critical Care, and Sleep Medicine, Baylor College of Medicine, Houston, TX, USA
diagnosis. As shown by other registries, idiopathic PAH was the common subtype of PAH with female predominance. Consistent with the REVEAL registry, this study showed a long lag between onset of symptom and diagnosis. A lack of distinctive clinical features, poor index of suspicion and a shortage of readily available medical care may account for the delay in diagnosis. In addition, a major challenge in carefully dissecting the PAH characteristics in the developing world also lies in the prevalence of many infectious diseases that can lead to pulmonary hypertension. Further, factors such as high altitude and other conditions such as undiagnosed rheumatic and congenital heart diseases may contribute to the PAH pathogenesis in the developing world.

In summary, the authors elegantly outline the characteristics of Saudi PAH patients and this data is of high clinical significance. This study could encourage other centers in the world to publish their data defining disease characteristics in their region so as to increase our global understanding of pulmonary arterial hypertension. It is well understood that better understanding of disease characteristics translates into an improved diagnostic and therapeutic approach. Therefore it is necessary to spread the word about PAH and actively initiate and participate in such studies.

REFERENCES

Corresponding Author
Zeenat Safdar, MD, FACP, FCCP
Associate Professor of Medicine
Director, Baylor Pulmonary Hypertension Program
Pulmonary-Critical Care Medicine
Baylor College of Medicine
Houston, TX 77030, USA
Email: safdar@bcm.edu
Abstract
Medical research in developing countries like Nepal is still in its infancy. Research activities conducted by medical schools and external funding agencies are focused mainly on infectious diseases due to their high prevalence, which means that research activities in the field of pulmonary vascular diseases (PVDs) are primarily focused in developed countries. As a result, there is currently not a single unit for conducting research on PVDs stationed in Nepal. Yet many Nepalese are continuously exposed to several underlying risk factors for the development of lung diseases, such as pneumonia, chronic obstructive pulmonary disease (COPD), asthma and interstitial lung diseases, all of which are very common in this country, and some of them are significantly associated with PVDs. Additionally, about 3% of Nepalese people living at high altitude are chronically exposed to hypoxia. To counteract this problem, the Excellence Cluster Cardio-Pulmonary System (ECCPS), Giessen, Germany and Agriculture and Forestry University (AFU), Chitwan, Nepal, decided to conduct research on PVDs based on common interests (Figure 1). Experimental setups for pulmonary vascular research are to be established. This will be further connected with medical schools and combine basic as well as clinical research.

Background
Nepal is a small Himalayan country and lies between the two giants India and China. Geographically it is situated at 26°12’ to 30°27’ N latitude, 80°4’ to 88°12’ E longitude and at various altitudes ranging from 70m above sea level to the top of the world. Many ecological niches rich in a variety of flora and fauna can be found across the country. The extensive geo-ecological diversity entices the biomedical scientists from all over the world to conduct research in this diverse arena. Although beautiful, Nepal, like any country, faces its shares of issues. Public health is amongst these concerns, as Nepalese people are still suffering from several infectious diseases. Although the burden of contagious diseases remains high, the non-communicable diseases are increasing, creating new challenges for the Nepalese health system, as the country-wide disease pattern is changing from contagious to non-contagious diseases. PVDs do not have geographic and socio-economic boundaries and as a result, many Nepalese people suffer from pulmonary vascular diseases. A lack of infrastructure and diagnostic facilities for different heart diseases means many potential pulmonary hypertension cases are hidden in the rural community, and therefore the exact prevalence rate is not known. Although no official data exists regarding the local magnitude of PVDs, several risk factors for the development of pulmonary hypertension abound in Nepal. The incidence of pulmonary problems is greater in urban area than in rural areas, reflecting the acquisition of several risk factors such as a sedentary lifestyle, consumption of fatty foods, obesity, smoking, air pollution etc. Although studies on pulmo-
nary diseases were conducted in Nepal, none of them focused on basic research. Only acute studies were carried out on mountain sickness or sildenafil trials in high altitude. The Ministry of Health and Population and the Government of Nepal have not yet formulated policies regarding pulmonary research in the absence of evidence-based findings. Thus it is urgent to address the issue of pulmonary diseases through research.

**Epidemiology of PVDs**

Nepal does not have a well-organized health facility for PVDs compared to developed countries. Proper databases for disease surveillance are scarce and pulmonary vascular diseases prove no exception. However, a recent hospital-based cross-sectional study on non-contagious diseases in Nepal showed that one third of the cardiac problems were associated with right heart diseases, which gives a clue for an indirect approximation of pulmonary hypertension prevalence within the country.

Seimetz et al showed that COPD is associated with the development of pulmonary hypertension. COPD is the most prevalent respiratory disease in Nepal and ranks in the first position among non-communicable diseases.

The reason behind such a high prevalence of COPD is likely due to the use of biomass fuel in traditional cooking stoves, the combustion of solid biomass fuels such as animal dung, wood, and crop residues, and air pollution from brick industries and old vehicles in the big cities. Additionally, the health hazards to housewives and workers in brick industries are likely underestimated in Nepal. The census 2011 report shows that more than 75% of households depend upon solid bio-fuels for domestic uses, which means near-constant exposure to many individuals. Furthermore, smoking is on the increase amongst younger Nepalese and the consumption of non-filtered cigarettes by elders could also attribute to a higher prevalence of COPD throughout the republic.

Nepal is a mountainous country and more than 3% of Nepalese people, predominantly Sherpa, are permanently living at high altitude. Most of the residents are well adapted to the high altitude environment, but many of the migrant people in northern Nepal are suscep-

---

Figure 1: Future scientific collaboration between Excellence Cluster Cardio-Pulmonary System (ECCPS) and Agriculture and Forestry University (AFU). Based and modified from the UN map of the World (Map No. 4170 Rev. 13, April 2012).
tible. There is an immense scope for conducting genetic studies among those populations. Moreover, local mammalian species e.g. yaks, pikas, and pandas are permanent dwellers in the Himalayan region. It would be worthwhile to screen these animals for hypoxia resistant genes.

**Prospective and Challenges**

Systematic studies on PVDs are still lacking in Nepal and there is no centralized database system. Some medical college teaching hospitals and government hospitals use a database system, but the software and format differ from hospital to hospital. This underscores an urgent need for an uniform recording and reporting format. Currently, most health institutions do not have a separate unit for pulmonary diseases where patients can receive good quality treatment. If such a unit was set up in different hospitals, database management would be significantly less complicated, and would create the opportunity for research activities. To this end, erecting a new research center will be crucial. Nepal has 17 medical schools, 7 national and regional hospitals, 14 zonal hospitals and 75 district hospitals, a statistic which holds fantastic potential for the establishment of a database system in order to conduct systematic clinical studies amongst the centers. Moreover, basic research on PVDs can be performed in collaboration with veterinary schools. Vet schools can provide an excellent platform for translational research using a number of laboratory animal models. To this end, we are designing a collaborative research set-up between ECCPS, Justus-Liebig University, Giessen, Germany and AFU, Chitwan, Nepal vet school (Figure 1) for translational research on pulmonary vascular diseases. Simple experiments will be carried out in Nepal and more advanced and sophisticated techniques will be conducted in Giessen, Germany. This collaborative approach will be a milestone for initiation of pulmonary vascular research in Nepal. As Nepal is rich in biodiversity, plenty of flora and fauna are available and we can focus our research on alternative medicine in PVDs. Additionally, research on acute as well as chronic exposure to high altitude can be carried out in Nepal, as every year several thousand Hindu pilgrims from India and Nepal visit a number of holy places, and many of them are susceptible to high altitude and develop mountain sickness.

In conclusion, Nepal is rich in opportunity with regards to the study of pulmonary vascular diseases, and with the start of this project, further studies will hopefully be initiated in the country, eventually leading to better resources, data and mortality outcomes.

**References**


**Corresponding Author**

Himal Luitel, PhD
Universities of Giessen and Marburg Lung Center Excellence Cluster Cardio-Pulmonary System Member of the German Center for Lung Research Giessen; Germany
E-mail: Himal.Luitel@innere.med.uni-giessen.de
Greece has been in the eye of the storm since the beginning of the global economic recession in late 2008, and the effects of the austerity measures on the Greek population have been severe. The healthcare and medical sectors in particular have been under strain. As a direct result of the financial crisis, the challenges for patients suffering from pulmonary hypertension have been augmented. Hellenic Pulmonary Hypertension (H.P.H) attempts to cope with these challenges and provide its members with information, mentoring, support and participation in various events.

Hellenic Pulmonary Hypertension is a non-profit organization established in 2013 by the initiative of patients with pulmonary hypertension. It is a voluntary association staffed with patients, caregivers, and friends, and its mission is to raise awareness of pulmonary hypertension in Greece; promote optimal standards of care and living for its patients; ensure the availability of all approved treatments and medicines; and represent its patients and protect their rights. H.P.H. is a member of PHA Europe and an affiliate of many European organizations for rare diseases.

The challenges we face due to the financial crisis are too many, too manifest, and too pressing, but there is no other option than to work hard and do the best we can.

The provision of healthcare in Greece has deteriorated as a result of the financial crisis. The Greek National Health System has had serious structural problems for a long time, but these problems have now intensified due to the harsh economic conditions and the austerity measures imposed since 2010. Reductions in public health expenditure, limited recruitment of health personnel, stricter monitoring on drug prescriptions, and continuous changes in healthcare services and the pharmaceutical market have had major impact on the provision of healthcare services, as well as dramatic consequences for all patients. As a result, the quality of life of patients suffering from rare diseases has been further reduced.

Patients with pulmonary hypertension in Greece have to overcome a number of obstacles. Firstly, access to diagnostic examinations in public hospitals has become more difficult. Regular diagnostic tests are necessary for close monitoring of the disease. The Ministry of Health has set various limits on the number and type of diagnostic tests that affiliated doctors can issue prescriptions for. Moreover, waiting lists have grown longer, and, as a result, in many occasions patients can wait up to three months before they have their diagnostic tests done.

Secondly, access to pharmaceutical products for patients with pulmonary hypertension has been problematic because of bureaucrat-
ic difficulties and long delays. The reason is that in order to reduce excessive prescription costs, prescription limits are imposed on each individual doctor. These limits mean that doctors who exceed an average monthly expenditure resulting from their prescribing may be called up to give further explanation. In simple words, doctors are allowed to prescribe drugs that cost up to €800 per month for each patient, while pulmonary hypertension drugs cost more than €5,000. Moreover, there are some practical obstacles that patients need to overcome to get their treatment. This is how things work: patients have to go to the drug-store month by month, and the pharmacist has to go through the same long bureaucratic procedure each and every time before giving the drugs. This is not only an exhausting and frustrating procedure for the patients, but also leads to long delays, as the time that elapses between the pharmacist’s call and the reception of the drug can sometimes be up to two weeks. The case is even worse for patients residing in provinces far from Athens or in the islands, and delays can be much longer. Our association is exercising pressure to get orphan drugs off the prescription limit altogether, because patients with chronic or incurable diseases should not go through all that trouble.

Another related problem is that uninsured patients face enormous difficulties to get their drugs. Until August 2014 – when an act was passed by the Ministry of Finance and the Ministry of Health – the high cost of drugs made it prohibitive for uninsured patients to take their treatment. The passing of the act was a positive measure, but it remains to be seen how it is going to work in practise because some practical problems remain unsolved. For example, it is still not clarified who the specialist doctor responsible to issue prescriptions (i.e. may he be a cardiologist or a pulmonologist?) is, and it is doubtful whether this doctor will be able to recognize this rare disease and be able to exceed the prescription limit, as PH specialists often do in order to preserve the patient’s life.

Thirdly, evaluations for disability pensions and allowances are not conducted properly. This is because PH patients are not evaluated by PH specialist doctors, but they appear before committees of doctors of random specialties. The problem is that these doctors are usually uninformed/misinformed about the rare disease of pulmonary hypertension. Taken together with the general mistrust that follows disability pensions and allowances in Greece, in most cases patients do not get what they deserve by law. There are also extreme cases of negative evaluations for some patients, meaning that their disability pensions are ceased and their pharmaceutical treatment is not covered. The evaluation procedure has also been a cause of frustration and disappointment for patients with pulmonary hypertension, as they have to argue with the committee about their ability to work or function properly in their daily activities.

The question then is what a voluntary non-profit organization can do to overcome these obstacles. The answer is simple: the best we can as this is about our survival. Our first and foremost priority is to protect the rights of our patients by exercising pressure anywhere we can, including the Greek government, European institutions, and the general public. Our mission, and truly our only weapon, is to raise awareness about the challenges and the obstacles we face. We have sought to raise awareness in three ways: through action, through participation, and through information. Here follows a list with our major achievements for 2014.

**Action**

- Working dinner with Minister of Health and other government and municipal officials.
- Organization of public activities and campaigns: H.P.H. organized a bicycle race for a second consecutive year in the center of Athens attracting numerous fans and so creating awareness of the disease.
- Creation of the “Tools of life”: a database that keeps record of the progress of the disease for each patient.
- Hosting patients from outside Athens and providing all patients in Greece with advice, mentoring, and psychological support.
- Production and distribution of a purple rib-
bon as a special symbol for PH to increase recognition of the disease.

**Participation**

- Help organizing medical seminars that bring together doctors from various specialties.
- Participation in all medical conferences, seminars and events related to PH in Greece and Europe.
- Cooperation and common action with other rare disease associations in Greece and Europe.
- Organization of events for patients, allowing them to meet, support as well as learn from each other, share their experiences, express their concerns and describe the problems they face.

**Information**

- “I learn about Rarity and I Live with it.” H.P.H. has set out an interactive program of education on rare diseases that will run in nursery, primary, and secondary schools aiming at early recognition of the symptoms and at increasing familiarity with rare diseases.
- Public awareness campaigns across Athens and in Thessaloniki, wherein our volunteers distribute information leaflets, balloons, pins, and hats about pulmonary hypertension.
- Frequent appearances in all mass media (health talk-shows in TV and radio, journals, social media).
- “Spread the Word about Rarity”: an informative newsletter which aims to bring rare diseases and their symptoms to the fore, to the benefit of both doctors and patients with rare diseases.
- Our own website (www.hellenicpulmonaryhypertension.gr)

Our association was established in the peak of the financial crisis, and, as of yet, we have managed to accomplish many things. However, H.P.H. was not established as a response to the financial crisis, and—hopefully—it will be still here after the crisis is over. Alas, there still remains so much to be done, and many are sadly beyond our reach. The problems we have been facing are not solely related to the crisis, although they have been certainly aggravated in the past six years. H.P.H. will continue providing its members with support, advice, and participation in events, in the hope that the cure will be found soon.

*Corresponding author: Ioanna Alissandratou*  
Head of Greek PH Patients & Caregivers  
H.P.H  
Mail box 52700, 145 72 Drosia Athens Greece  
E-mail: info@hellenicpulmonaryhypertension.gr

Figure 2: An image from the ‘Get Breathless for PH’ rally, which took place April 2014.
Abstract
We present the case of a 71 year old man with pulmonary arterial hypertension (PAH), atrial fibrillation, and monoclonal gammopathy of undetermined significance (MGUS), who experienced sudden left periorbital headache, left eyelid ptosis and ophtalmoplegia, with intact pupillary reflexes. The patient was treated with bosentan and sildenafil citrate. The sildenafil dosage had been recently doubled to 40 mg tid. Thorough laboratory and radiologic investigation for the cause of the palsy was negative. Sildenafil was withdrawn and six months later there was complete resolution of symptoms and signs. Sildenafil might have been a potential cause of reversible III cranial nerve palsy in this PAH patient.

Introduction
Sildenafil citrate is a selective phosphodiesterase type-5 (PDE-5) inhibitor, and has a proven therapeutic efficacy in male erectile dysfunction (ED). In 2005 it was shown to be effective in and gained approval for pulmonary arterial hypertension (PAH) treatment. Despite the fact that 20 mg per os tid is the approved regimen, the optimal dose for PAH is titrated and often a higher dosage of sildenafil is prescribed in numerous countries. Pupil sparing III cranial nerve (oculomotor) palsy has been twice reported in men with occasional use of sildenafil for ED. To our knowledge, we present the first case of pupil sparing oculomotor nerve palsy in a patient with PAH who was taking sildenafil on a regular basis. The patient’s medical history was positive for monoclonal gammopathy of undetermined significance (MGUS), a disease with documented risk for arterial and venous thrombosis and with occasional reports of cranial as well as peripheral nerve palsy.

Case Report
A 71 year old man with a previous diagnosis of atrial fibrillation and PAH presented in our clinic claiming sudden onset of diplopia, left eyelid ptosis and ipsilateral periorbital headache, two weeks after having doubled sildenafil’s dosage. Two years before the incident, the patient was referred to our PH service due to deteriorating dyspnea on exertion (New York Heart Association functional status - NYHA III). A detailed diagnostic work-up was performed and after right heart catheterization [RHC, mean pulmonary artery pressure (mPAP): 35mmHg, pulmonary arterial wedge pressure (PAWP): 10mm Hg, pulmonary vascular resistance (PVR): 5 Wood units] and a thorough exclusion of other causes of pulmonary hypertension (with emphasis on left heart and thromboembolic disease), the diagnosis of pulmonary arterial hypertension (PAH) was confirmed, and treatment with bosentan initiated. During the diagnostic work-up, a single protein band in the gamma region of serum protein electrophoresis was revealed (IgG kappa chains). Bone marrow biopsy was positive.

Aikaterini Flevari1, Iraklis Tsangaris1, Stylianos Argentos2, Dimitrios Konstantonis1, Irini Mavrou1, Stylianos E. Orfanos1, Ioannis Lekakis2, Apostolos Armaganidis1

1Second University Department of Critical Care and Pulmonary Hypertension Clinic; 2Second University Department of Radiology; 3Second University Department of Cardiology and Pulmonary Hypertension Clinic; ATTIKON General University Hospital, Haidari, Athens, Greece
for low grade plasmacytosis (<10%); hematological, biochemical and radiological investigation excluded Multiple Myeloma (MM) and the diagnosis of monoclonal gammopathy of undetermined significance (MGUS) was also set. Although the patient initially responded well to treatment, a year later he was re-admitted due to deterioration of clinical status (NYHA status late III and leg edema), while his hematological disease was stable. A new RHC was performed (mPAP: 43mmHg, PAWP: 7mm Hg, PVR: 8 Wood units) and sildenafil (20mg per os tid) was then added. Four months later due to poor clinical response, the dose of sildenafil was doubled (40mg tid) and fifteen days later the patient experienced a dull left periorbital pain, which was mildly relieved with paracetamol. The following day, he had blurred vision, diplopia and gradually deteriorating ptosis of the left eyelid. He was then admitted to our clinic. On admission, his vision was clear and near visual acuity was normal. There was ptosis and slight abduction of the left eye (Figure 1) with a deficit in adduction beyond midline (Figure 2). There was also complete limitation of left eye elevation and depression. Pupils were equal in size and pupillary direct and indirect reflexes in dim and bright light were normal. An anterior segment exam, a dilated fundus exam and a neurological exam all revealed normal results. Likewise, the arterial blood pressure and pulse rate were within normal range. Both brain computed tomography (CT) scan and magnetic resonance imaging (MRI) tests were negative. His hematological condition revealed a mildly elevated glycosylated haemoglobin, (HbA1c: 6.4% with upper limit 5.6%), but fasting glucose and
plasma lipid profile were within normal limits (glucose: 85mg/dl, cholesterol: 150 mg/dl, triglycerides: 130 mg/dl, LDL: 102mg/dl and HDL: 32mg/dl). Atherogenic Plasma Index (AIP=0.07) revealed a low cardiovascular risk. Lumbar puncture showed normal cerebrospinal fluid electrolytes and normal cytology. Sildenafil was gradually withdrawn and three months later the patient had an important improvement in eyelid ptosis and in all ophthalmic movements but adduction. Six months later, left ophthalmoplegia was fully restored.

Discussion

Sildenafil citrate causes selective PDE-5 enzyme inhibition, thus maintaining high values of intracellular cyclic guanosine monophosphate (cGMP), the second messenger of nitric oxide (NO) and principal mediator of smooth muscle vascular relaxation, especially in penile and pulmonary vasculature. It thus regulates blood flow in these regions, minimally affecting other areas of the body. Since 2005, it joined prostanoids and endothelin receptor antagonists in the therapeutic armamentarium of PAH. Sildenafil’s most common side effects include flushing, headache, dyspepsia and nasal congestion, which occur in 6-18% of subjects depending on dose, and which result from systemic vasodilation, secondary to PDE-5 inhibition of vascular smooth muscle. Major ocular adverse events are associated with the increase in retinal and choroidal blood flow, due to the wide expression of PDE-5 in these tissues. Also due to co-inhibition of PDE-6 enzyme, in rod and cone photoreceptors, the retinal phototransduction pathway is impaired and it may be responsible for mild and transient visual effects, such as blue tinged vision or increased photosensitivity.

Third (III) cranial nerve palsy has been reported in association with PDE-5 use in two cases. The first reported case was a 56 year old man, who developed a complete pupil-sparing III nerve palsy 36 hours following a single sildenafil dose intake (50mg) for erectile dysfunction. In both cases, authors considered that sildenafil might have caused transient hypoperfusion of the III cranial nerve. In all cases, including ours, pupillary light reflexes were intact, which indicates that parasympathetic fibers controlling sphincter pupillae muscle via the ciliary ganglion were not damaged. This can be attributed to the anatomical arrangement of its fibers, as fibers controlling pupillary function travel on the superficial area and are spared from ischemic injuries. Indeed, in the majority of ophthalmic neuropathies of vascular etiology (e.g. diabetes mellitus), centrally located fibers are affected, while pupillary fibers are spared.

Although there was a temporal association of sildenafil dosage increase with the nerve palsy followed by full recovery after sildenafil discontinuation, we cannot exclude that other conditions might have played a role. For example MGUS, a premalignant usually asymptomatic plasma cell disorder that affects at least 3% of adults older than 50 years carries an augmented risk for both arterial and venous thrombosis. There have been a few reported cases connecting MGUS to cranial nerve palsies, specifically Bell’s. In these reports, blood flow in the nutrient vessels of the nerves (vasa nervorum) was considered impaired due to blood hyperviscosity caused by the circulating abnormal protein.

Conclusion

Sildenafil may be a potential etiologic factor for reversible third cranial nerve palsy. Although it cannot be explicitly proven that sildenafil was the cause of this patient’s neuropathy, the close temporal relationship between the drug’s dose augmentation and patient’s symptoms, as well as the full recovery after sildenafil withdrawal, strongly suggests this possibility.

References


Corresponding author:
Dr. Aikaterini Flevari
Second Department of Critical Care
Attikon Hospital
1 Rimini St, Athens, Greece, 12462
E-mail: kflevari@gmail.com

The first official 2015 PVRI Fundraiser is as above. Tickets are now available at https://uk.patronbase.com/Gulbenkian/Sections/Choose?prod_id=PVM1&perf_id=1
Interview with a patient suffering from pulmonary arterial hypertension

The physician’s view on a patient suffering from pulmonary hypertension (PH) is pretty clear: What is their systolic pulmonary arterial pressure, their mean pulmonary arterial pressure, and their pulmonary vascular resistance? How far can she/he walk? What is her/his NYHA status? To which group of PH does she/he belong and what medications is she/he taking? When was the disease diagnosed and is the patient stable? These are simple questions that characterize and subsequently pigeonhole a patient for further treatment.

Rarely do we ask ourselves how patients look at their disease and their view on doctors.

This interview with a PH patient tries to shed some light on the patient’s view on living with pulmonary hypertension. The patient is a 49 year old woman, married, with two dogs and no children.

When and how did the disease start?
It started around 2000 when I noticed shortness of breath while climbing stairs and during my daily work. I worked as a social worker with young girls and was responsible for their recreational activities. I was travelling with them to foreign countries, but the travels were becoming more and more exhausting. At the beginning I thought the limitations were due to my getting older, as I was reaching my forties by then. However, when the shortness of breath increased, I went to my family doctor who sent me to several specialists.
lips, and my general condition deteriorated so
much that I had to be admitted to the hospital.
I had to stay there for 3 months and got many
examinations, including a left heart catheter.
Finally the nurse told me that my heart was very
sick and there was no hope; I should prepare for
death.

Was there a diagnosis from the doctors?
As far as I remember, no. They just said that
they could not do anything for me.

How did you react?
By then I had been ill back for quite some time,
so I believed the doctors were right, and I pre-
pared my last will and patient’s provision.

How did your family react?
My husband was very shocked and was with me
the whole time. However, he and my sister did
not accept what the doctors had said. Fortu-
nately my sister is a physician, so she searched
for a specialist where I could go for a second
opinion. She talked to Professor Olschewski
and Professor Ghofrani, pneumologists at
the University of Giessen, who told her that I
should come to them immediately.

What happened in Giessen?
I was admitted to the ward and had to stay for
a few days where they performed a right heart
catheterization and diagnosed pulmonary hy-
pertension.

Who told you about the diagnosis and how did
you realize what it means?
It must have been the doctors who gave me the
diagnosis, but I cannot remember any details. In
the hospital I shared a room with a woman of a
similar age to me who had been diagnosed with
PH some years before. She explained everything
to me. I was very lucky to have her as my
roommate. In addition, my husband collected
everything that he could get from the internet.
Later I joined a PH patients’ organization to
gather more information.

How did your family and friends react when they
heard about the disease?
They were very supportive. Friends helped me
by walking my dogs during that time as I could
not do it myself; the girls from my group where I
previously worked designed posters saying: “Go
on…”, “Don’t give up”. My husband attended to
me all the time. We have now been married for
32 years and went through this together.

What treatment was initiated after diagnosis
and how did your condition change?
Treatment started with sildenafil and phenpro-
coumon in 2002. After reaching a dose of 3x50
mg per day, I felt slowly better and could be mo-
bilized. However, after being in bed for several
months, it was a very long time before I could
walk and exercise again.

Did you experience any side effects of the medi-
cation?
From taking phenprocoumon I had very strong
periods - so strong that eventually my uterus
had to be removed. This was okay with me as it
was recommended that I avoid pregnancy due
to my PH. Later in 2012 I had “phenprocou-
mon shock”. I got blisters filled with blood all
over my body, including on my face. My family
doctor told me that I could no longer tolerate
phenprocoumon, and I stopped taking it.
Once sildenafil was officially approved for PH,
my medication should have been exchanged
with a sildenafil-containing drug with a differ-
ten name. However, I was very satisfied with
my old medication. After some trouble with my
health insurance, it was finally accepted that I
could continue to take the drug that I was used
to.

What was the further development of the dis-
 ease?
I was quite satisfied and in stable condition. In
2004 I participated in an ongoing clinical study.
Since then I have not experienced any deteriora-
or worsening of the disease.

How are you currently limited in daily life?
I retired soon after my diagnosis. Due to my
limited physical condition at that time it was no
problem to receive a disability pension. Current-
ly, I am feeling quite well. I go for a daily walk
with my two dogs for three to four hours. I do
not look sick and sometimes my friends forget
that I am limited in exercise. When they ask
me if I want to go hiking with them, I have to
remind them that this will be a very slow hike. I
can exercise a little bit; however, I avoid climb-
Are you in contact with other PH patients?
I joined a PH patients’ organization in order to gather information about the disease. Unfortunately, I never went to one of the meetings. Sometimes patients that live close to me get my address from the organization and get in touch with me, but otherwise I am not involved in their activities so much. Currently, I am having big trouble with my health insurance because they no longer want to pay the transport to Giessen. The patients’ organization provided me with a lawyer who is helping me with the trial against the health insurance. Next month we have a date at court.

How did your family doctor react when he found out about the diagnosis?
He was a little bit ashamed, because he had to admit that he thought I was a malingerer. He had never heard of PH before and had no idea about the disease. However, he educated himself and now is in close contact with the doctors in Giessen. Whenever I have to take new medication or have any problem, he calls Giessen to ask for advice.

Is there any advice that you want to give to anybody?
I am lucky to still be alive. Fortunately, my sister is a physician and she searched for treatment options. Also it was great luck that I came to Giessen and the medication worked well. One of the worst experiences was the ignorance of the doctors at the beginning of the disease, before my diagnosis was set. I want to tell doctors that they should listen better to their patients and not put them in pigeonholes too early...

Corresponding Author
Dr. Natascha Sommer, MD, PhD
Department of Internal Medicine,
Justus-Liebig-University Giessen,
Universities of Giessen and Marburg Lung Center
Member of the German Center for Lung Research
Giessen, Germany
E-mail: Natascha.Sommer@innere.med.uni-giessen.de

PVRI CHRONICLE

CALL FOR PAPERS

PVRI Chronicle needs your help to grow.

Please encourage your junior physicians, medical students, graduate students and post doctoral fellows to contribute case reports, interactive discussion articles, fellows activities, Did you Know facts, PVD images and book reviews, and don’t hesitate to submit your own!

Convinced?
Then please submit your work to:
Sachindra Joshi at sachindraraj_joshi@nymc.edu
and Nikki Krol at adminpvri@gmail.com

Thank you!
Dr Lan Zhao (LZ): It is a great honor to interview Professor Xiancheng Cheng on this occasion during the PVRI annual meeting. Professor Cheng was my mentor in the late 1980s when I was in China. He is retired now, but he still plays a significant role in the field of pulmonary vascular diseases in China. I would like to take this opportunity to ask Professor Cheng to tell about his life in this field, and of course the history of PVDs in China.

First of all, I will ask Professor Cheng to start with a brief introduction of himself, and to also tell us the early history of the clinical and experimental research of pulmonary vascular disease in China.

Professor Xiansheng Cheng (XC): Thank you, Dr Zhao, for your interview. I am sorry that I do not speak English very well. So I will do the interview in Chinese.

I was a graduate student in 1963 in Fuwai, and my project was focused on “the changes in gases and acid-base balance of blood in patients with cor pulmonale”. This led my research on pulmonary vascular disease and hemodynamics and became my lifetime career. In 1972, the Health Minister of the Chinese government assigned me to lead a team, consisting of 6 doctors, to establish the first workgroup of Cor Pulmonale. This then progressed as the first Pulmonary Vascular Disease Center in China. The workgroup focused on the prevention, diagnosis and treatment of cor pulmonale (or pulmonary heart disease) in China, including the diagnosis by ECG, chest X-ray, echocardiography, blood gases and acid-base and pulmonary function testing. We also took great interest in the hemodynamics of cor pulmonale caused by COPD at rest and during exercise, and defined the patients as the “dominant pulmonary hypertension” and “latent pulmonary hypertension or latent cor pulmonale”. The latter includes the contemporary concept of “exercise-induced pulmonary hypertension”. Then the National Collaborative Network of Pulmonary Heart Disease was established, and I served as the general secretary of the organization. In the past 25 years, seven pulmonary heart disease conferences have been held for exchanging experiences in research on hemodynamics and right heart function, as well as clinical studies. Indeed, it has been 40 years in total since the beginning of our efforts in the fields, and we have been awarded prizes for our contributions and achievements in China.

In the 1980s, we started to work with the obliterative pulmonary hypertension. In 1986 we got the grant from the “seventh five-year plan” of the Chinese government, which covered two parts: study on primary pulmonary hypertension (PPH), and chronic thromboembolic pulmonary hypertension (CTEPH). We performed hemodynamics and acute vasodilation tests (nifedipine sublingually), and drug efficacy in 115 obliterative pulmonary hypertension (46...
CTEPH and 69 PPH). We found that about 20% patients suffered from an elevation in pulmonary pressure rather than a pressure decrease during testing, which validated the hemodynamic test before taking calcium channel antagonists. Meanwhile, we also investigated the relationship between hemodynamic index and pathology of congenital heart disease associated with pulmonary arterial hypertension. The open lung biopsies were performed in 81 patients with indication of borderline for surgery operations- among these patients, we had 59 patients with pathological lesions I-II/IV grades, and 11 of them had bidirectional shunt and cyanosis and they were still operable.

In 1985, I got the WHO scholarship and started my study with the famous pulmonary vascular pathologist, professor Wagenvoort, in the Netherlands. With him, I studied the morphological changes included in the plexiform lesions in PAH associated with congenital heart disease and pathological changes in pulmonary vessels in rheumatic valvular diseases. I found endothelial cell proliferation and medial hypertrophy, and that luminal narrowing occurred generally in the early stage. Along with the disease progression, vascular smooth muscle cells disappeared with extensive endothelial and medial fibrosis. My result indicated that vasodilators had no effects in these irreversible vascular lesions. When I came back to China, I instructed my student Dr. Zhi-Hong Liu to explore the collagen deposits in vascular walls and medical intervention for the process in the pulmonary vessels, and concluded that the structural changes may be the pathogenesis of pulmonary vascular disease which is now recognised as vascular remodeling. From then on, I extended my research from the PH caused by COPD to a larger scale, including the functional and structural change in the whole pulmonary circulation and right ventricle.

I wrote a book in 1993 entitled Pulmonary Vascular Diseases. I developed my theory on the definition of pulmonary vascular disease, with the concept that the structural and/or functional disorders of the whole or local pulmonary circulation are due to primary or secondary pulmonary vessel lesions. In 1991, based on the 241 in-patients with PVD in my hospital, I...
proposed a new classification system of PVDs including both large and small vessels, arteries and veins, congenital and acquired disorders. Unfortunately, until now, there is no classification of PVDs in the world. I suggest that PVRI should take a broader view to explore the whole pulmonary vascular disorders and establish the classification of PVDs.

Professor Wagenvoort suggested the small vessel lesions are divided into seven categories: type 1, plexogenic arteriopathy; type 2, thromboembolic PVD; type 3, pulmonary venous hypertension PVD; type 4, pulmonary veno-occlusive disease; type 5, hypoxic pulmonary hypertension PVD; type 6, pulmonary vascular changes due to lung disease; type 7, pulmonary vascular changes associated with reduced blood flow. Each class contains a large spectrum of different disorders of pulmonary arteries and veins. These definitions and classifications are not complete, however, it is of importance in helping us form a thorough understanding of the extent of the field of pulmonary vascular diseases. We should take a broad view to observe the whole pulmonary circulation and right heart function, rather than focus on only the pulmonary arterial hypertension or pulmonary embolism, since the field contains hundreds of unexplored diseases and it also requires interdisciplinary knowledge for doctors and scientists in the field, especially the cardiologists and pulmonologists. For these reasons, I would give an example of Professor Fishman, a former president of American Heart Association. He was not only an expert in cardiology, but also a respiratory physiologist, and he wrote an excellent book called The Pulmonary Circulation: Normal and Abnormal.

LZ: Thank you very much for your introduction of PVD in China, what a fascinating history as well as the story of your lifetime contributions. You began your research on cor pulmonale in the 1970s, and gradually progressed into the “world of PVDs”, especially the pulmonary embolism research in 1980s. I appreciate very much your concept from 1991 that we should take a broad view in the PVD field, and pay attention to the right heart function, and the importance thereof for the new classifications of PVDs. I hope these ideas will give the doctors and scientists in the field a new vision for the future, indeed, the interdisciplinary combined efforts of cardiologists and pulmonologists are important for an in depth understanding of PVDs. Could you please tell us a bit more about the development of PVDs in the recent 10-15 years?

XC: As mentioned above, on the basis of our previous work in the 1970s-1980s, in the 1990s we carried out research on pulmonary embolism (PE) sponsored by National Key Project in China, which contains studies on COPD, PH, and PE. In the 2000s, the Chinese government supported the research further, and included right ventricular dysfunction into the National Key Project, paying great attention to the field of PVDs. In 2013, Chinese government issued its new grants plan and “The Molecular Mechanism and Intervention of Pulmonary Hypertension” is listed as the top priority on the projects of National Natural Science Fund. The period from 1970s to 1980s was really a tough time. My views were not accepted by the Chinese Association of Cardiology or the Chinese Association of Respiration. Recently the situation has changed, there are two workshops of PVDs in China, one of which belongs to Chinese Association of Cardiology, while the other belongs to Chinese Thoracic Society.

LZ: In recent years, you have actively participated in the international conferences and discussions. I am very impressed by your enthusiasm, you have always come up with your own opinion based on your years’ of clinical and experimental experiences. Especially, I want to mention...
XC: My concept of “right ventricular system” derives from the basic fact that the survival of patients with left heart diseases are mostly depending on their right ventricular function rather than left ventricular function deterioration. CHD-PAH patients have a significantly better prognosis than IPAH patients because they have better right ventricular function. Therefore, the research on the mechanism of right ventricular adaption and the compensation which integrated with pulmonary circulation is very important. Meantime, the left ventricle contributes to about 20-40% of right heart function, and the other 30-50% pressure in right ventricle was completed by Interventricular septum. So when we explore the right ventricular function, we must take into consideration the influence of the left ventricle, Interventricular septum, and pericardium. It is a integrative system centered on the right ventricle, that covers a good co-ordination of interdependence between ventricles, right ventricle-pulmonary circulation unit, biventricular “motor” of interventricular septum, and pericardium.

LZ: I have read your book and I am sure it will impress and help a lot of doctors in China. In recent years, you played an active role in the PVRI and attended most of the annual meetings. You have not only brought the advanced knowledge back to China, but also exchanged your ideas and experience with experts from all over the world. Could you please talk about your experience with the PVRI?

XC: As I have mentioned, I started my researches on PVDs in the 1970s. At that time, no attention was paid to this field, and some works we made were unrecognized, and I felt like an orphan who was fighting alone without understanding or support. I have always dreamt to find a place to belong. Fortunately, five years ago, I got to know the Pulmonary Vascular Research Institute (PVRI), I finally found my family, and I was so excited. My experiences and research have finally found a place – the expertise in the PVRI understood and recognised me, and I joined the organization. I attended the 3rd and 6th meetings of PVRI and I began to advertise PVRI in China: I wrote an article to introduce the principle, structure, research area and the nature of PVRI in China Medical Tribune. I care about the Institute. I think it is my responsibility to support organisations like the PVRI. Compared to the Lisbon meeting in Portugal, in the Istanbul meeting I witnessed a tremendous progress of the PVRI, in its management, co-ordination, content and the multi-disciplinary involvement. I wish that the Institute will develop well and I hope PVRI will take a wider scope including PVDs and right ventricular diseases. In addition, I heard that the Excellence Cluster of Cardio-Pulmonary System (ECCPS) was established in Germany, and that reflects a trend towards the integrated system of the cardio-pulmonary system. I want to emphasize that pulmonary hypertension consists of heterogenous entities which contain complex processes in aspects of etiology, pathogenesis, clinical features, diagnosis, treatment and prognosis. By creating comparisons between these diseases, I believe that we could find the common pathway in the disorders and cure the disease by targeting it. I think PVRI has started to take strategic vision about the development of the field, and it has put the focus on understanding the pulmonary structural remodelling, the coordination of multiple disciplines and the training of the next generation in the field. I believe these will promote the rapid development of PVRI. In summary, to me the PVRI is like a warm family and I sincerely hope it will further develop into a great academic society that will promote better understanding of the disease. It will play a leading role in the PVD world. Finally, thank you Dr Zhao for your interview.

Corresponding Author
Nikki Krol
PVRI Executive Administrator
PVRI Chronicle Executive Editor
Canterbury, Kent
United Kingdom
E-mail: nkr@pvri.info
PVRI BOARD OF DIRECTORS & ADVISORS MEETING, BAD NAUHEIM, GERMANY, 27 JANUARY 2014

The Board of Directors and Advisor (BODA) meeting took place at the Dolce Hotel in Bad Nauheim, one day prior to the 8th PVRI Annual General Meeting and the 7th Scientific Workshops and Debates. Attended by Board members Stuart Rich, PVRI President Sheila Glennis Haworth, Ghazwan Butrous, Ahvie Herskowitz, Bert van den Bergh, Ardi Ghofrani, Martin Wilkins, Declan Doogan, Simon Campbell, Maha al Saud and Pascoal Mocumbi, the meeting was also open to member-representative Dr Antonio Lopes, PVRI Executive Administrator Nikki Krol and Pulmonary Circulation Executive Editor Christina Holt. This year also saw the introduction of Mrs Stephanie Barwick, appointed PVRI Chief Executive. Dr Stuart Rich acknowledged BODA member Professor Magdi Yacoub’s recent achievement. Professor Yacoub was awarded the ‘Order of Merit’ by the Queen of the United Kingdom, the highest ranking UK achievement which is awarded to only a few outstanding individuals.

Topics covered at the BODA meeting included a review of the finances and the upcoming First Drug Discovery & Development Symposium. Professor Ghazwan Butrous stepped down as PVRI Managing Director, and the BODA unanimously voted for him to adopt the honorary title of PVRI President Emeritus to thank him for his many achievements and accomplishments for the PVRI.

An overview of these subjects was presented to the membership at the Annual General Meeting.
Board of Directors & Advisors Meeting, Bethesda, USA, 15 July 2014

Attended by PVRI President & Chair Sheila Glen-nis Haworth, Stuart Rich, Ghazwan Butrous, Martin Wilkins, Declan Doogan, Bert van den Bergh, Ahvie Herskowitz, Paul Corris, and Stephanie Bar-wick, the meeting reviewed the topics previously discussed in Bad Nauheim six month prior. Stuart Rich was thanked for his years as Chairman of the Board, and all that PVRI had accomplished due to his tireless dedication. This included the First Drug Discovery and Development Symposium which had taken place only days earlier, and was unani-mously considered a great success by the present BODA members. The PVRI internal regulations were discussed, as was the latest on Pulmonary Circulation, the PVRI Strategic Plan 2015-2018 (now available on the PVRI website), membership and registration fees, PVRI branding and logos, and the newly christened ‘8th PVRI Annual World Congress’ in Guangzhou, January 2015. Time was also given to the definition of Professor Ghazwan Butrous’ new role as President Emeritus, and the locations of future PVRI Annual World Congresses.

8th PVRI Annual General Meeting & 7th Scientific Work-shops & Debates, Bad Nauheim, Germany, 27-31 January 2014

For the 8th PVRI Annual General Meeting and 7th Scientific Workshops and Debates, the Pulmonary Vascular Research Institute joined with the ECCPS Symposium Molecular Mechanisms and Treatment of Lung Disease. Congratulations are due to the ECCPS and their administrative staff for organising such a beautifully detailed meeting in the Dolce Hotel. Housing 25 Conference rooms, the Dolce is an impressive business hotel with a solid reputation, and PVRI members, ECCPS members, and other attendees were well-served throughout the week of meetings and socializing.

The meeting started in earnest on Tuesday January 28th, with the PVRI Pre-Symposium on Lung Vascular Compliance and Recruitment, chaired by David Badesch and Anna Hemnes. These included ‘Right heart after load at rest and exercise*’, by Robert Naeije, Brussels; ‘PA stiffness and right ventricular-PA coupling’, by Rebecca Vanderpool, Pittsburgh; and ‘Detection and evaluation of the potential for lung microvascular recruitment in PAH’, by David Langleben, Montreal. Those who followed the meeting from home and afar were treated to a steady stream of images, updates, and streams of consciousness from the PVRI Twitter and Facebook social media, and each new speaker was immortalized on the web with their name and topic under the hashtag #PVRI14.

Enjoying this recap? To read the full report from page 4, see link: http://pvrifiles.s3.amazonaws.com/PVRI_Publish/PVRI_Chronicle/Volumne%201%20Issue%202/Finished%20PDF/Final%20Chronicle%20V1I2.pdf
Taking into account the increasing interest in Latin America for Pulmonary Hypertension (PH), largely due to the Continuing Educational Programs in different Latin American countries on pulmonary hypertension in general and specifically in children in Colombia, the PVRI Paediatric Task Force saw it fit to organize the First Latin American Symposium on Pulmonary Hypertension in Children in Colombia.

During the Symposium on PH in Leh, Ladakh (India) in August 3-7 2012, with Dr. Alicia Marquez (Pediatric Cardiologist), we had a meeting with Professor Ghazwan Butrous. In this meeting we agreed to organize the First Latin American Symposium on Pulmonary Hypertension in Children in Colombia. This idea had the immediate approval and support of the PVRI and the Colombian Society of Cardiology, whose President, Dr. Efrain Gomez, decided to provide all the administrative support for its organization. Then the dates and place of this event were defined: Hotel Hilton in Cartagena de Indias on February 21 and 22, 2014. For the development of the project, the great collaboration of Dr Ghazwan Butrous and Dr Sheila Glennis Haworth (current President of the PVRI) was very important. Together with Dr Ian Adatia (Alberta University, Edmonton Canada), Dr Antonio Augusto Lopes, Head of Pediatric Cardiology, Heart Institute (INCOR), Sao Paulo Brazil, Dr Maurice Beghetti, Head of Pediatric Cardiology, University of Geneve, Geneve Switzerland, Dr Maria Jesus del Cerro, Head of Pediatric Cardiology, Centro Especial Ramón y Cajal, Madrid España and Dr Julio Sandoval Head of research, Instituto Nacional de Cardiologia de México, México DF, they immediately accepted to collaborate as speakers. With Professor Haworth’s collaboration, the first draft was set up. Each of the speakers contributed to the program, that covered the different topics related with PH in children, from the newborn (Persistent Pulmonary Hypertension of the Newborn), to the adult with PH related with congenital heart disease. A lecture by Migdalia Dennis, President of the Latin Society of PH for patients, was included in the final program.

The Symposium was burdened with two objectives: 1) to increase the interest in PH in children in Latin America and 2) to promote the research in this interesting topic, with the central issue being the importance of early detection of PH to avoid the pulmonary vascular disease. This was a crucial aspect, and was reflected in the Logo of the Symposium, in which you can see the sentry box of the Cartagena walls that represent the Pulmonary trunk, which give origin to the pulmonary branches with pulmonary vascular disease; complications that we need to avoid. To promote the research, we gave great relevance to the Poster Session that was included in the scientific program. As an incentive, we funded a monetary prize to the five best posters. The organization of the event required hard work for one and a half years.

The Symposium began with a simple opening ceremony on February 20 at 7:30 PM in Hilton Hotel near the beach. There were short talks from Dr. Gabriel Diaz, President of the Symposium, Dr. Efrain Gomez, President of the Colombian Society of Cardiology and Professor Sheila Glennis Haworth, President of the PVRI. After that, there were cocktails and a sample of the typical Caribbean dances.

The scientific program began Friday the 21st at 8:00 AM and ran until 6:00 PM with active participation of 147 participants (mainly Pediatric Cardiologists and Pediatric Neumologists) from different countries, such as Argentina, Brazil, Chile, Peru, Ecuador, Venezuela, Honduras, Mexico, USA, UK, and Colombia.

After a welcome by Dr Efrain Gomez, Professor Ghazwan Butrous opened with the presentation...
entitled ‘Global impact of pulmonary vascular diseases: the role of the Pulmonary Vascular Research Institute.’

He was followed by Dr Ian Adatia, who presented ‘Definition, Classification, Epidemiology.’ The final session before the coffee break was presented by Professor Haworth, and entitled: ‘Aetiology and pathophysiology: Importance of early detection of pulmonary hypertension.’ The next three sessions focused on making a comprehensive diagnosis in young people, and was kicked off by Dr Antonio Augusto Lopes with his presentation ‘Noninvasive diagnosis of pulmonary hypertension.’ Then Dr Ian Adatia presented ‘Cardiac catheterization and CT scan,’ followed by Professor Haworth with ‘Exercise testing.’ Dr Julio Sandoval focused his lecture on ‘Biomarkers- MRI en HP en ninos,’ after which there was time for questions.

At noon, a two-hour Poster Session with 34 posters from different countries. The reviewers were the invited speakers and they selected the top five. After the excellent poster session, presentations continued in the session entitled ‘Pulmonary Hypertension Related with Hypoxia and Altitude.’ The first lecture was by Dr Julio Sandoval, who presented ‘Hypertension pulmonar idiopatica,’ and was followed by Dr Maria del Cerro with ‘HPPRN-HP y displasia broncopulmonar.’ This was followed by Dr Gabriel Diaz ‘Hipertension pulmonar y altura S.N.M.,’ with Dr Liliana Moreno bringing up the rear with the unrecorded ‘Hypoxia induced pulmonary hypertension in rodent models, genomics and intervention strategies.’

The final session of the day focused on the current routine management of pulmonary hypertension. Dr Antonio Augusto Lopes presented a well-received lecture entitled ‘Endothelin receptor antagonists.’ He was followed by Dr Ian Adatia, whose work focused on ‘NO and phosphodiesterase inhibitors.’ Finally, Dr Julio Sandoval rounded off the day with ‘Prostaglandinas y atrioseptostomia en ninos.’

At 7 PM there was an elegant dinner supported by one of the sponsors, in the chapel of the Santa Clara Hotel (former Convent of the Poor Clares) in the beautiful Colonial Cartagena de Indias (inside the walled city).

On Saturday 22nd, the Scientific Program began at 7:00 AM with a work breakfast and despite the early hour, there was active participation of around 110 attendants. The central topic discussed was how to organize nets and registry on PH in Latin America, based on the experience of speaker Dr Maria Jesus Del Cerro from Spain. This will be the basis for the development of the registry of the PH in Children in Latin America. To this end, Dr Ian Adatia presented ‘Acute post-operative pulmonary hypertension,’ whilst Dr Antonio Augusto Lopes focused on ‘Pulmonary hypertension in adults with congenital heart disease: the Eisenmenger syndrome and other problems,’ Professor Sheila G. Haworth contributed with ‘Establishing clinical networks within and between countries to care for children with pulmonary hypertension,’ which was followed by an emotional presentation of PVD patient Migdalia Denis, President of the Latin Society of PH, entitled ‘La Sociedad Latina de Hipertension Pulmonar. Su importancia para padres y pacientes.’ After an unrecorded lecture from Dr Maurice Beghetti, the Scientific Program ended with PVRI President Professor Sheila G. Haworth’s hopeful ‘Pulmonary Hypertension: the Future.’

It is important to note the consistent attendance of the participants to every session, so that the conference room was always full. As such, we consider the First Latin American Symposium on Pulmonary Hypertension in Children a complete success. The two objectives demarcated at the beginning of the project were fulfilled, and the participants and the speakers were satisfied.

This First Symposium on Pulmonary Hypertension in Children will be the basis for continuing the work on PH in Children in Latin America in the future, as we continue our attempt to attain the two objectives: to increase the interest on Pulmonary Hypertension in Children, and to promote the research in this interesting topic. To this end, we will organize this Symposium every two years. The proposed next location is Buenos Aires, Argentina, in 2016. Dr Dora Fabiana Haag was nominated as President of the Symposium.

To see an overview of all the recorded conference talks at the Cartagena Symposium, please go to: http://pvri.info/meetings/1st-latin-american-symposium-ph-children-cartagena-de-indias-february-22-23-2014#.VInDUfl_v1E
Dr Antonio Lopes presents at the First PVRI Latin-American Symposium on Pulmonary Hypertension in Children, Cartagena de Indias, Colombia.

Professor Ghazwan Butrous, Professor Sheila Glennis Haworth, and Dr Ian Adatia smile during the Symposium, 22 February 2014.

Mouth-watering local cuisine on display.

Delegates listen to the conference talks, some using headphones to hear the translation.

Dr Gabriel Diaz, a very active member of the PVRI Paediatric Taskforce, addresses the audience.

Learning by day, dancing by night: traditional dancers put on a show during the First PVRI Latin-American Symposium on Pulmonary Hypertension in Children.
This year the SAPH 2014 Conference, also known as the Saudi Association for Pulmonary Hypertension and the PVRI Eastern Mediterranean Region 7th Annual Joint Pulmonary Hypertension Assembly, took place in Muscat, Oman. Spanning three days from May 1st to May 3rd, the program promised sessions on classifications and updates, new developments in PAH therapy, insights in pulmonary hypertension due to left heart disease, a detailed look at CTEPH, management challenges in PAH patients and pregnancy challenges in PH patients, as well as practical clinical scenarios and more specific PAH management particularities, such as pericardial effusion and CTD associated PAH- and it certainly delivered. As usual with SAPH, the high quality scientific program was accompanied by a flawless and aesthetic organisation, this year in the Ritz Carlton Al Bustan Palace in Muscat, Oman. A jewel on the coast of Oman, the hotel is situated right on the beach, whilst some of the rooms are located right at the edge of the pool- a near necessity in a country where May temperatures reach well into + 45C. The meeting kicked off on such an evening, when the temperatures rose high outside and attendees retreated into the cool blast of the hotel airconditioning. After registration, which included name tags, PVRI/SAPH pins and non-alcoholic cocktails, attendees took a seat in the impressive ballroom. The Opening Ceremony included a welcome from Conference Chairman Dr Saleh Al Dammas, followed by an introduction to PVRI by PVRI President Sheila G. Haworth, an introduction to SAPH by Head of SAPH Majdy Idrees, and a more detailed look at the program from Head of SAPH Scientific Committee Abdullah Al Dalaan. Then followed the talks, focusing on ‘Classification & Updates’, chaired by Drs Mohamed Al Hajjaj and Saleh Al Dammas. These presentations covered the basic physiobiological and genetic aspects of pulmonary arterial hypertension, and were spearheaded by Professor Ardeschir Ghofrani, FPVRI, with ‘PH phenotypes: Distinct Inflammatory Pathways’. Originally due to give two talks, Professor Stephan Rosenkranz, FPVRI had a change in schedule which meant he would leave earlier than expected. As such, he combined both talks ‘Pulmonary Vascular Changes in PH Due to Left Heart Disease: Closer Look at the Histopathological Level’ and ‘Insight into RV assessment: Size and Function as Predictors of Clinical Worsening (Echo & MRI)’ into one, entitled ‘Pulmonary Vascular Changes Due to Left Heart Disease’, a two-part talk which can be found at the link. His presentation was followed by Professor Ghazwan Butrous, who provided an update on the genetics of PH.

If you enjoyed this short recap, please note that the full text with recorded conference talks is available pp. 13-16 in PVRI Chronicle Vol 1, Issue 2. The journal can be found on the PVRI website at: [PVRI_Pu Publication/PVRI_Chronicle/Volumne%201%20Issue%202/Finished%20PDF/Final%20Chronicle%20V1I2.pdf](http://pvrifiles.s3.amazonaws.com/PVRI_Publication/PVRI_Chronicle/Volumne%201%20Issue%202/Finished%20PDF/Final%20Chronicle%20V1I2.pdf)
Professor Majdy Idrees presents on the mission of the Saudi Association for Pulmonary Hypertension (SAPH).

PVRI Chief Executive Stephanie Barwick poses with the PVRI promotional materials.

From left, Drs. Manal al Hazmi, Maha al Dabbagh and Nazarreno Galie chair a session at the SAPH conference.

Attendees, including PVRI CEO Stephanie Barwick, PVRI President Sheila G. Haworth, and PVRI Executive Administrator Nikki Krol, listen to the presentations.

‘Best Abstract’ winner Dr. Stephen Chan (second from left) stands with (from left to right) Professor Ghazwan Butrous, SAPH Conference Chairman Saleh al Dammas and Dr. Abdullah al Dalaan.

A group photo of the speakers and attendees of the SAPH Conference in Muscat, Oman, 1-3 May 2014.
First Meeting of the Central Asia Task Force, Bishkek, Kyrgyzstan, 16-17 June 2014

This first meeting of the Central Asia (CA) Task-force was held in conjunction with the ‘International Forum Multidisciplinary Approach to the Diagnosis and Treatment of Cardiorespiratory Diseases’. This ensured that as many people as possible learnt about pulmonary hypertension and pulmonary vascular diseases and about the PVRI. There were approximately 150 participants, from Kyrgyzstan, Kazakhstan, Mongolia and Uzbekistan, of whom 25 were already interested in the PVRI. It was a conventional programme including speakers from Saudi Arabia (Majdy Idrees), Austria and Portugal (President of the European Society of Cardiology) but the most rewarding session was a roundtable in which representatives from the CA republics told of their experience in managing patients with PVD in their own country.

The problems they encounter are similar to those in all developing countries; lack of awareness and teaching in pulmonary hypertension and PVD, consequent late referral, poor management, poor access to expensive medicines, inadequate treatment and follow-up. In addition, high altitude pulmonary hypertension is a major problem in Kyrgyzstan, Tajikistan and Mongolia (Western Mongolia). In these countries a large percentage of the population either lives permanently at high altitude or is semi-nomadic, spending the summer months at altitude with their flocks.

There is no infrastructure, no clinical networks, and

PVRI Annual Get-Together at the American Thoracic Society meeting, San Diego, USA, 19 May 2014

PVRI held their traditional annual Get-Together meeting during the American Thoracic Society (ATS) conference in San Diego on May 19th from 9-11 pm. Hosted by the W Hotel, the get-together was attended by 30 PVRI members. Hosted right in the middle of the weeklong ATS Conference, the mini-break was timed perfectly to allow members a chance to recharge their batteries and PVD enthusiasm amongst similar ilk. Importantly, the meeting was also an unique chance to meet old and long-time no-see friends. Although there was no official talk, all PVRI members exchanged their valuable experiences, those related to the science and research in the field of the pulmonary vascular diseases, as well as those related to everyday life. The majority of attendees were younger PVRI members, supported by the renowned and leading experts in the field such as professors Drs. Ralph Schermuly, Norbert Weissmann and Werner Seeger- a heartening reminder of the PVRI’s durability and capacity for growth.

The PVRI Get-Together event also proved an excellent opportunity for the PVRI Young Council to hold a separate 30 minute meeting. During this time, new members Drs. Natascha Sommer and Oleg Pak were welcomed into the fray by other Young Council members, and introduced themselves with a small summary on their scientific and academic background.

A full overview of the Get-Together is available in the PVRI Chronicle, Vol 1 Issue 2, p. 17, or at the link:

Professors Talant Sooronbaev and Majdy Idrees laugh together at the PVRI Central Asia Task Force meeting.
no physicians or nurses specifically trained to care for this patient group. Several also acknowledged that they had equipment, such as echocardiography machines but no staff trained to use them properly. Few had access to cardiac catheterisation facilities, although several admitted that there were catheter labs used by cardiologists for coronary arterial studies.

All the republics have had problems transferring from the Soviet Semashko system of health care to their own new model. The Soviet polyclinic system remains. All confessed that following independence they had made quite good progress but that they had now ‘got stuck’, usually due to lack of funds. There are significant financial differences between republics. All are poor except Kazakhstan. Kazakhstan has two well-funded cardiac centres, in Almaty and Astana. Cardiac transplantation is carried out in Astana.

The Way Forwards for PVRI CA

1. The leaders of the Task Force are Talant Sooronbaev and Almaz Aldashev.
2. It was agreed by the physicians from Kyrgyzstan, Kazakhstan, and Mongolia that they need to identify centres which would become centres of excellence in pulmonary hypertension, not more than two in each country, each to have a named leader. These centres would build a referral network within each country. They will need our support in lobbying their Ministers of Health for financial support.
3. The leaders of each country would form the CA Task Force Committee.
4. All the Round Table participants acknowledged the lack of awareness and the consequent lack of expertise in diagnosing and managing patients with pulmonary hypertension, in all countries. All welcomed the suggestion of holding master classes in pulmonary hypertension. The venue, date and financing of this initiative is to be arranged and the plan/programme needs much thought and consideration if it is to meet local needs. Majdy Idrees agreed to help plan the master classes, having recently undertaken a similar exercise in Saudi Arabia.
5. The participants agreed that they need:
   - National patient registries primarily to understand the burden of disease in the hospital system and the distribution of the various aetiologies of pulmonary hypertension in their population. Registries form the resource for clinical research studies
   - Diagnostic and treatment algorithms for pulmonary hypertension
   - A protocol for right heart cardiac catheterisation with acute vasodilator testing, noting that NO is not available to them with the possible exception of Kazakhstan
   - Protocol for atrial septostomy
6. The Task Force members would like to take part in clinical trials but expressed their need to establish a firm, stable, sustainable infrastructure first.

The Task Force for CA was formed at the request of the two leaders Talant Sooronbaev and Almaz Aldashev. They and the physicians from Kyrgyzstan, Kazakhstan, and Mongolia who took part in the PVRI Roundtable discussions were enthusiastic about taking this initiative forwards. Talant Sooronbaev and Almaz Aldashev are in touch with interested physicians in Uzbekistan, Tajikistan and Turkmenistan who either could not get a Kyrgyzstani visa or were not allowed to leave their country. Although none of the republics can be said to have a centre of excellence in pulmonary hypertension Professor Aldashev and Professor Sooronbaev have considerable clinical and research experience in high altitude pulmonary hypertension. Professor Aldashev has collaborated with Professor Martin Wilkins at Imperial College London for 10 years and their research programme continues to expand. Thus the leaders of the CA Task Force have a long standing interest in pulmonary hypertension and their desire to develop a knowledge base and a rational way of managing the patients in CA is a logical progression. The PVRI is in a position to help them achieve their goals and we should support them as best we can.
The First Annual Drug Discovery and Development Symposium for Pulmonary Hypertension was held in Bethesda-Washington DC on July 14 and 15th this year. Leading scientists in the field of pulmonary vascular disease, right heart failure, and clinical trial designs joined members of the pharmaceutical industry and regulatory authorities to discuss identifying the most prominent promising treatments for future development in this field. The purpose of this symposium was to serve as a unique forum for stakeholders interested in the treatment of pulmonary vascular diseases for sharing cutting-edge science with the input of international thought leaders.

The meeting was highly successful. Over 100 people attended, and enjoyed provocative presentations followed by spirited discussions. From the session on pulmonary vascular diseases we heard about novel targets with the potential for disease modification based on addressing abnormalities on underlying inflammation, genetic modifications, and vascular proliferation. From the session on right heart failure we heard of innovative approaches towards preserving right ventricular function by addressing metabolic abnormalities, beta blockade, and gene transfer techniques. The session on clinical trials opened ideas on ways to develop new therapies that are better targeted, and that might require smaller clinical trials with higher success rates.

The attendees left feeling energized about the prospects of breakthrough therapies being developed in this field over the upcoming years. The PVRI and the FDA were gratified that the goals of the meeting were accomplished and are looking forward to having this annual event next year.

The program is as included below. Please note all those highlighted in blue can be found as recordings on the PVRI website (www.pvri.info). If you are reading this in digital format, please simply click on the link to view.

**Day 1 (July 14th 2014)**

**Session 1: Pulmonary Vascular Disease**
- State of the Art Review: Changing the paradigm- Refocusing our approach to treating pulmonary vascular disease, Marlene Rabinovitch
- Focusing on inflammation and immune modification to treat pulmonary hypertension, Paul Hassoun
- The potential of histone deacetylation inhibitors for pulmonary hypertension, Martin Wilkins
- Genetic modification- Inhibitory RNA and epigenetics, Sebastian Bonnet

**Session 2: Approaches to Right Ventricular Failure in Pulmonary Hypertension**
- State of the Art Review: Novel therapeutic approaches to preserve the right ventricle, Serpil Erzurum
- Metabolic therapies for right ventricular failure in pulmonary hypertension, Evangelos Michelakis
- Beta blockade of the right ventricle in pulmonary hypertension. Learning lessons from the left, Anton Vonk Noordegraaf
- Gene transfer of SERCA2a to the pulmonary vasculature and right ventricle, Jane Leopold

**Day 2 (July 15th 2014)**

**Session 3: Clinical Trials: Changing Our Approach to Drug Development**
- Keynote Lecture: Developing new therapies with better efficacy: Following the lead of our oncology colleagues, Patricia Keegan
- Imatinib for pulmonary arterial hypertension. Failed therapy or failed trial design? H. Arde-schir Ghofrani
- Tacrolimus for pulmonary hypertension. Approaching the disease using high throughput screening of BMPR2 mutant animal models, Roham Zamanian
- Summary of experimental trials in progress, and opportunities for a collaborative approach to solving the need for valid clinical biomarkers, Tim Moore
- Symposium summary: Action plan for the upcoming year, Stuart Rich and John Newman
3rd PVRI International Leh Symposium ‘Ventilation and circulation in hypoxia: From mechanisms to patients and back’, Leh, Ladakh, India, 19-23 September 2014

The third International Leh Symposium 2014, ‘Ventilation and circulation in hypoxia: From mechanisms to patients and back’ took place in Leh, Ladakh, J&K, India from September 19-23. Leh, which is located at 3500 meters of altitude, forms an ideal venue for organizing such meetings. The first scientific session commenced on 20 September 2014, this was followed by eleven more sessions in subsequent days. Each session was based on a topic relevant to high altitude (HA) and hypoxia. The focus of the first day of the meeting was on the clinical aspects of acclimatization, (mal) adaptation and therapeutics.

Among the various talks, the presentation and subsequent discussion on pilgrimage at high altitude generated a lot of interest among the audience, which included PVRI President Elect Professor Paul Corris. It was acknowledged that how the pilgrims, army men, mountaineers and trekkers were different from each other in terms of their physical as well as mental tempaments. It specifically raised the question of psychological drive over physiological. This diversity makes them respond differently under the same hypobaric hypoxic stress. This could certainly be a new dimension to HA research. Subsequent sessions focused on clinical aspects and discussed common medicines like Diamox (acetazolamide), oxygen requirement and availability, intermittent hypoxia that are the important defenders of HA illnesses. Along with the current line of treatment, the need to develop better therapeutics was emphasised. Clinical and physiological features of highland population were also elaborated mainly concentrating on adaptation and diseases.

The second and third day presentations were more inclined towards the molecular aspects of hypoxia. Erythropoietin (Epo) and hypoxia-inducible factors (HIFs) have been always the molecules of interest when studying hypoxic effects; hence, their characteristic involvement and successive triggering of downstream biomolecules was discussed in (mal) adaptation especially in high-altitude pulmonary edema (HAPE) and pulmonary hypertension (PH). Exercise capacity and limitations, sleep and PH at HA were some other topics. The speakers focussed on Epo, HIF1α, HIF2α, telomere and telomerase, IL-4, IL-13, right ventrical dysfunction and treatment. Here, pulmonary hypertension, being the hallmark of HA illnesses, was discussed thoroughly. In addition, the involvement of miRNA in HAPE along with genetic and biochemical markers that interplay in HAPE pathophysiology was highlighted. Our co-host SNM Hospital (Leh) also participated with presentations from senior physicians of the hospital, who showed some upcoming areas of research at HA. They specifically em-

Left side, posters attended by the participants at the Poster session. Right side, two young researchers, who received the best poster award are seen with the poster evaluation committee team.

Inauguration: Top from extreme left, Tsering Norboo, Youngchan Dolma, Buddha Basnyat, Peter Wagner, Qadar Pasha and Max Gassmann. Bottom, self introduction of participants on the first day of the meeting.
phasised on the exaggeration of dormant infection on arrival to HA, which was very well detailed with pictures of affected organs from deceased patients. Differential gene expression in healthy sojourners, thrombosis crisis at HA, Epo expression under hypoxic condition, role of iron in erythropoiesis and hypoxia-regulated iron homeostasis were also among the other topics, that were very well appreciated in the symposium. The experienced researchers and clinicians through their insightful talks shared their wealthly experiences and knowledge with the young researchers, who participated enthusiastically and contributed scientifically through their talks and poster presentations.

The poster presentation initiated a wave of curiosity and enthusiasm among the young researchers and also among the senior scientists and clinicians. It also helped the young researchers to define their work more meticulously. The posters discussed varied topics, among these few needs mention; such as, development of nano drug delivery system, characterization of pre-synthesized angiotensin-converting enzyme inhibitor on spontaneously hypertensive rats, another interesting study show-cased the designing and development of a highly economical but sensitive assay to detect breast cancer using aptamer, a study showed that the reason for hypertension at highland was more haematological (hematocrit and erythrocytes) compared to the lowland risk due to increased triglycerides and VLDL; among the other high altitude posters: the role of various kinases with respect to SNS signalling and significance of telomere shortening and telomerase were highlighted in HAPE pathophysiology and adaptation, two genome wide association studies with regard to HAPE and systemic hypertension in Ladakhi natives identified few loci. Posters were displayed all through the symposium. The poster session committee selected two posters for the best poster award. Telomere work was adjudged the best and the kinases the second best.

The symposium provided a perfect stage for interaction between and among the renowned scientists, young researchers and clinicians especially from the local SNM hospital in Leh. The scientific discussions over the cup of coffee and lunch were highly enjoyable and scientifically insightful. These interactions put forth collaborative studies among the high altitude scientific community and the faculty at SNM hospital, which will definitely help in strengthening the HA research to achieve global solution to HA adaptation and disorders. The suggestions were also on how we could make this symposium more popular and improve even better. The emphasis was also on to encourage a lot of young researchers around the world into HA studies as HA has the answers to lot of unaddressed questions not only with respect to HA illnesses but to various other pulmonary and respiratory diseases in which hypoxia is explicitly involved. Hotel Grand Dragon, the venue, arranged a Ladakhi cultural program that was enjoyed by all. It was followed with a sumptuous dinner to conclude the day. The discussions on the last day were encouraging, but with useful and highly critical suggestions by the participants. It was followed by visit to recently established HA research centre at SNM hospital. The symposium concluded with vote of thanks and the announcement of the 4th International Leh Symposium 2016 under the leadership of Prof. Talant Sooranbaev in Issyk-Kul, Kyrgyzstan.

The awareness created by the three international Leh symposia has helped us achieve our ambition in the form of establishing a Research Centre at SNM Hospital. The role of the medical superintendent Dr. Dolma and the senior physician Dr. Ghulam Mohammad of SNM hospital with Dr. Qadar Pasha, the organizing secretary, IGIB is appreciable. With this centre, we provide the basic infrastructure required to carryout the desired research at this altitude to tackle the scientific problems. This facility is for the use of the faculty of SNM Hospital as well as the international clinicians/researchers working on hypoxia, who forge collaboration with Indian researchers, too would avail the facility.
The sessions are on: presentations by the delegates

Students at Registration desk on day 1 of Leh Symposium 2014

The audience participates in the question-discussion hour after a session

Delegates of Leh Symposium 2014 pose happily for a group photo
PVRI Regional Task Forces

Saudi Association for Pulmonary Hypertension and the PVRI Eastern Mediterranean Region (EMR) Task Force

Task Force Leaders
Paul Hassoun, USA
Majdy Idrees, KSA

Task Force Members
Janet Ajuluchukwu, Nigeria
Gulnaze Mahomed Arif, Mozambique
Rosie Burton, South Africa
Maha Al-Dabbagh, Saudi Arabia
Albertino Damasceno, Mozambique
Ana Olga H. Mocumbi, Mozambique
Okechukwu S. Ogah, Nigeria
Karen Sliwa, South Africa
Adriana Mario Francisco Tivane, Mozambique

Initiatives
SAPH has continued to expand its activities quite rapidly. It is now recognized regionally and somewhat internationally for its services in the field of pulmonary hypertension (PH). The number of active members has also risen steadily during the last 5 years, reflecting the success of SAPH in building more awareness and creating a positive environment between physicians and healthcare providers. Interestingly, more nurses, paramedics, and patients are now involved in different SAPH activities.

Educational events/meetings
The following scientific and educational activities have taken place in 2014:
• The 7th annual conference for EMR (SAPH 2014), May 2014. Muscat, Oman
• The 9th Pediatric Master class in PH. February 2014. Riyadh, KSA
• The 10th Adult Master class in PH. October 2014. Riyadh, KSA
• Awareness Day for PH for internist & family physicians
  • March 2014. Riyadh, KSA
  • June 2014. Jeddah, KSA
  • October 2014. Dammam, KSA
• Awareness Day for nursing and health care providers
  • April 2014. Riyadh, KSA
• Awareness Day for PH for public
  • May 2014. Jeddah 2014
• PH Family support Day
  January 2014. Jeddah, KSA

Publications
• Hussam Sakkijha, Majdy M. Idrees. Pulmonary hypertension due to lung diseases and/or hy-
Provence of Saudi Arabia
• Inhaled Iloprost for severe pulmonary hypertension in COPD patients.
• Genetic studies in Saudi patients with congenital heart disease
• Bronchiectasis & PH in Saudi patients
• Prevalence of PH in the high altitude in Saudi Arabia
• Prevalence of chronic thromboembolic pulmonary hypertension (CTEPH) in Saudi Arabia
• Contribution in the PVRI consensus statement for the management of pulmonary hypertension in the developing world
• Other initiatives
• SAPH/EMR is establishing a further collaboration with PHA Europe and PHA Canada
• SAPH/EMR is planning to expand its collaboration and share experiences through working with the PVRI Central Asia Task Force, PHA South Africa, and many early initiatives/groups in North African countries

Goal Summary 2015
1. To hold the 8th Annual Joint (SAPH/PVRI) meeting in Abu Dhabi, UAE on April 9-11 2015. For more information about this meeting, please visit the conference website (www.saph2015.com) or the SAPH website (www.saph.med.sa)
2. To organize the yearly pediatric PH master class in February and the Adult PH master class in October 2015
3. To continue holding frequent awareness days in different regions in the EMR region
4. To participate in World Pulmonary Hypertension Day on 5 May 2015
5. SAPH has signed an agreement with Bayer Pharma to conduct 21 awareness sessions in Saudi Arabia and different Gulf countries throughout 2015
6. SAPH will work with the UAE pulmonary hypertension group to conduct serial training sessions in order to establish the first PH center of excellence in Abu Dhabi

Research activities
Current research includes:
• The prevalence of pulmonary hypertension (PH) in Sickle-cell disease in the Eastern

The PVRI Central Asia Task Force

Task Force Leaders
Almaz Aldashev, Kyrgyzstan
Talant Sooronbaev, Kyrgyzstan

Task Force Members
Chakima Achmedova, Tajikistan
Begench Anaev, Turkmenistan
Abay Baigengin, Kazakhstan
Elena Kovzel, Kazakhstan
Irina Kozlova, Kazakhstan
Nurridin Maragapov, Kyrgyzstan
Erkin Mirrakhimov, Kyrgyzstan
Murat Mucarov, Kazakhstan
Batyr Osmonov, Kyrgyzstan
Aleksey Pak, Kazakhstan
Jury V. Pja, Kazakhstan
Diloram Rachimova, Uzbekistan
Ulan Sheraliev, Kyrgyzstan

Initiatives
The PVRI Central Asia Task Force brings together leading experts in the field of pulmonary hypertension from the countries of Central Asia (Kyrgyzstan, Kazakhstan, Mongolia, Uzbekistan, Tajikistan). Its main mission is the education of physicians and the general population; pulmonary vascular disease research; the implementation of new methods for the diagnosis and treatment of pulmonary hypertension (PH); to improve the quality of care; and ultimately to better the quality of life of patients and reduce mortality.

Educational events/meetings
- Participation in the 7th Congress of PVRI and the creation of the Central Asia PVRI Taskforce 27-31 January, Giessen (Germany)
- The 1st International Symposium of the PVRI Central Asia Task Force was held in Bishkek, June 16-17 2014. During the symposium, a collaboration was formed between the leading experts from Kyrgyzstan, Kazakhstan, Uzbekistan, Tajikistan, Mongolia and Russia and Saudi Association for Pulmonary Hypertension (SAPH) President Majdy Idrees, as well as Chief Executive Stephanie Barwick and President Sheila G. Haworth of the Pulmonary Vascular Research Institute (PVRI). The following resolutions were adopted:
  - Identify centers and leaders who are engaged in the pulmonary hypertension area
  - Create PH Centers of Excellence in each country as represented by the number of individuals
  - Train 3 specialists (pulmonologist, cardiologist, pediatrician) for each PH Center of Excellence (for echocardiography and RHC) with support from the PVRI
  - Develop PH clinical guidelines for developing countries with a consideration for regional and local features
  - Develop a register of patients with PH
  - Certification of PH Centers of Excellence and participation in international clinical trials with support from the PVRI

Members of the PVRI Central Asia Taskforce, in the middle Professor Talant Sooronbaev.
PH Educational programs and training for physicians
Create patient organizations of pulmonary hypertension
Provide pulmonary hypertension patients with necessary medications (via state support)
Organize seminars and workshops in field of PH in each country within the framework of national and international forums
Seek support from pharmaceutical companies and partnerships
Professor Sooronbaev T.M. represented the PVRI Central Asia Task Force at the ‘Third International Leh symposium 2014’ in Leh, Ladakh, India, in September 19-23, 2014. Prof. Sooronbaev presented on high altitude pulmonary hypertension (HAPH) and respiratory disease at high altitude.
The PVRI Central Asia Task Force met in Astana (Kazakhstan) with the participation of leaders in the field of PH from Russia, Kyrgyzstan, Kazakhstan and Uzbekistan.

Other initiatives
- Dr M. Mirrahimov organized a PH Center of Excellence at NCCIM, which will provide the following:
  - selection and training of specialists
  - provision of equipment and basic drugs
  - improving the quality of medical care in PH
  - maintenance of a register to allow regular monitoring of patients with PH
- Develop clinical guidelines for PH (to be presented and discussed at a workshop on EBM in Bishkek)
- Provide training for physicians and patients
- Kyrgyz - Swiss joint study “HAPH Register”
- Development of regulatory documents and the inclusion of basic drugs for PH in state support program through the HIF

Goal Summary 2015
1. To hold the 2015 Symposium of the PVRI Central Asia Task Force in Astana, Kazakhstan.
2. To create a PVRI Central Asia Task Force PH Centre of Excellence in Bishkek, Kyrgyzstan, which will provide the following:
   - master classes and workshops on Doppler echocardiography for 3 specialists (pulmonologist, cardiologist, pediatrician) from each country represented in the Task Force, 6-9 April 2015.
   - Educational courses for physicians in the field of pulmonary hypertension in Bishkek, Kyrgyzstan, 10 April 2015.
3. To organise joint studies and publication of their results in the PVRI peer-reviewed journal Pulmonary Circulation.
4. To ensure participation of experts from Kazakhstan, Kyrgyzstan and other Central Asian countries in the annual PVRI congress, in 2015 in Guangzhou, China.
5. Further develop and publish the PH clinical guidelines for developing countries.
the Pulmonary Hypertension Registry of Kerala, supported by the Cardiological Society of India and co-ordinated by Professor Harikrishnan and Professor K Kumar. They aim to collect data on 3000 patients in the first year.

1. The following projects continue, funded by GSK: Genetic insights into Idiopathic Pulmonary Arterial Hypertension in India, lead by Professor Nallari at Osmania University and Dr BKS Sastry in Hyderabad

2. Does non-regression of pulmonary hypertension following balloon mitral valvotomy correlate with BMPRII mutations? Lead by Professor Harikrishna in Trivandrum

3. Telomeres in adaptation and maladaptation under hypobaric hypoxia lead by Professor Qadar Pasha, Institute of Genomics and Integrative Biology, Delhi

4. Molecular mechanisms of pulmonary microvascular endothelial dysfunction under fluid shear stress, lead by Professor C. C. Kartha, in Trivandrum

Goal Summary 2015

1. Dr Sastry is organising a meeting early in 2015 to plan activities for the coming year.

PVRI India Task Force

Task Force Leaders
BKS Sastry, India
Paul Corris, UK

Initiatives
Professor Harikrishnan has been a very successful Task Force leader of PVRI India and PVRI Review Editor-in-Chief. Unfortunately his heavy workload obliged him to resign as Task Force leader in August. The PVRI is grateful for his un-failing support. He has been replaced by Dr BKS Sastry, known to many of you as an authority on Idiopathic Pulmonary Arterial Hypertension. He is based in Hyderabad. In addition, Professor S. G. Haworth will be replaced by Professor Paul Corris, Newcastle-on-Tyne, UK.

Educational activities
The High Altitude Task Force under Qadar Pasha lead a meeting in Leh, Ladakh in September, in collaboration with PVRI India. This was a truly international meeting of high calibre and was an outstanding success.

Research activities
The PROKERALA study is a new initiative. This is
The PVRI Sub-Saharan Africa Task Force

Task Force Leaders
Karen Sliwa, South Africa
Ana Mocumbi, Mozambique

Task Force members
Friedrich Thienemann, South Africa
Kemi Tibazarwa, Tanzania
Taiwo Olabisi Olunga, Nigeria
Gerald Maarman, South Africa
Sandra Pretorius, South Africa
Kamilu Karaye, Nigeria
Sani Mahmoud, Nigeria
Ogah Okechukwu, Nigeria
Dike Ojji, Nigeria
Patience Udo, Nigeria
Amam Mbakwem, Nigeria
Moshood Abiodun Adeoye
Albertino Damasceno, Mozambique
Elijah Ogola, Kenya
Jean-Baptiste Anzouan-Kacou, Ivory Coast
Isaac Kofi Owusu, Ghana
Bertrand Ellenga Mbolla, Congo
Anastase Dzudie, Cameroon

Initiatives
The PVRI Sub Saharan Africa Task Force has been involved with a number of projects and collaborative meetings this year, including a scientific and research day, a visit to Douala General Hospital, and joint clinics.

Educational events/meetings
- 1st Collaborative Meeting, Maputo, 20-23 November 2013
  Professors Karen Sliwa and Ana Mocumbi were invited to participate in the Mozambique-South Africa Joint Workshop held at Pequenos Li-bombos Dam, Maputo Mozambique.
  The workshop was organized by the Fundo Nacional De Investigacao (FNI), as part of a partnership agreement between the two countries.
  The opening lecture was given by Dr Antonio Leao, Executive Director, FNI (Mozambique), followed by a lecture by Dr Aldo Stroebel, Executive Director, National Research Foundation South Africa. They gave overviews on the research infrastructure of the countries and the rationale for increasing the partnership, the aim of which is to form knowledge-based societies.
  The workshop included lectures showcasing joint partnerships in the areas of agriculture, environmental research and health aspects.
  Professor Mocumbi, Dr Thienemann and Professor Sliwa were invited to give a joint lecture, providing an overview on cardiovascular research carried out by their teams. They covered a number of topics, including pulmonary hypertension in general, pulmonary hypertension due to left heart disease and specific aspects of managing pulmonary hypertension in pregnancy. Dr Thienemann and Professor Sliwa

Lecture to a broad audience of physicians at the Cardoso Hotel.
also met with researchers and clinicians from Eduardo Mondlane University who are now participating in the PAPUCO Registry. Professor Sliwa also met with Professor Alberto Damasceno and his team to discuss the BEHAF study, including updates on recruitment and retention. Professor Damasceno actively participates in this important study and has already recruited 16 patients.

• 1st Collaborative Meeting, Maputo, April 2014

Professor Karen Sliwa and Priv. Doz. Peter Zartner participated in several activities in the week 6th to 11th April 2014.

1. Professors Karen Sliwa (South Africa), Alberto Damasceno (Eduardo Modlane University, Maputo, Mozambique), Ana Mocumbi (National Health Institute, Maputo, Mozambique) and Priv Doz. Peter Zartner (Germany) were invited to give lectures at an educational workshop, held on 9th April at the Cardoso Hotel, Maputo. The workshop was endorsed by the Mozambican College of Cardiology and was attended by more than 80 cardiologists, gynaecologists, general physicians, surgeons and paediatricians. This 5-hour workshop included lectures on congenital heart disease and appropriate interventions, general heart failure management, hypertensive crises and also covered specific aspects of heart failure occurring in pregnant women. Funding for this meeting was provided by the South African National Research Foundation (NRF) and the Fundo Nacional De Investigacao Mozambique (FNI), as part of a partnership agreement between the two countries, Sanofi Aventis and the Heart Failure Society of South Africa (HEFSSA). The workshop also included lectures showcasing joint partnerships in the areas of heart failure, tackling congenital heart disease, as well as pulmonary hypertension.

2. Professors Mocumbi, Damasceno and Priv Doz Zartner held joint clinics, evaluating a number of cases with congenital heart disease. The aim was to evaluate these cases for possible cardiac catheterization and intervention. Several cases were screened and two patients were booked for cardiac catheterization. This was supported by a generous donation by the company NuMED Inc., Hopkinton, NY, USA, and PFM, Cologne, Germany, who donated a number of cardiac catheters, balloons and devices for this times interventions and for future visits to Maputo.

3. Professor Sliwa also met with Professor Alberto Damasceno and his team to discuss the BEHAF study, including updates on recruitment and retention. Professor Damasceno actively participates in this important study and has already recruited 25 patients. The team consisting of Drs Inácio Ribaué, Celia Novela and Valério Govo discussed challenges with recruitment, case report forms (CRFs) and other related aspects at a meeting and dinner.

4. Professor Sliwa visited Professor Ana Mocumbi’s new research site at Mavalane Hospital, where she had the opportunity meet the team (Dr Naisa Manafe, Dr Fauzo Valá; nurses Fulgência Simião and Rosália Nhachengo; undergraduate student on rotation Delfina Chachuaio) and to learn about their various research which covers aspects of cardiovascular disease presentation at this secondary level.

Delegates at the 1st Collaborative Meeting, Maputo. Attendees carefully listen to the presentations.
hospital, research in heart failure related to HIV, the recruitment of patients into the pulmonary hypertension cohort study (PAPUCO) and other research activities. Professor Mocumbi highlighted their research on the use of echocardiography and ultrasound screening at secondary level hospitals, which is part of the NIH-Fogarty IMEPI-funded scheme.

**Other initiatives**

Report on attendance to the first scientific and research days of the Douala General Hospital and hospital visit, Cameroon, October 2014

I was extremely fortunate to be invited as a guest of honour to give a keynote lecture, as well as chair sessions at Cameroon's First Scientific and Research Day (2 October, 2014) in Douala, Cameroon, by the Medical Director of Douala General Hospital, Professor Henry Luma, and the Director-General, Professor Eugene Belley Priso.

**Scientific and Research Day**

The aim of the day was to highlight the importance of evidence-based clinical practice by the presentation of a number of research projects performed in Cameroon. After the official opening ceremony, lectures were given on a number of different topics, including trends in admission and mortality in patients admitted for heart failure at Douala General Hospital, development of a simple prediction algorithm on asthma and the epidemiology of thunderclap headache. The meeting was attended by 200 delegates, including general physicians, surgeons, obstetricians, cardiologists, endocrinologists, registrars and medical students, who participated very actively throughout the day. I gave lectures on the differential diagnosis and importance of cardiac disease in pregnancy and important causes of maternal mortality, as well as on peripartum cardiomyopathy in Africa. These lectures led to intensive discussions on an appropriate referral algorithm and risk stratification for women in low-income countries, such as Cameroon. Posters were presented during the lunch breaks and winners were selected. I chaired the afternoon session which was dedicated to research methodology.
universal health coverage and therefore not everyone has access to medical facilities.

Social Programme
I am grateful to Professors Luma and Priso who put together a wonderful evening programme at Mangrove Restaurant, as this provided me with an opportunity to talk to many staff members, as well as colleagues visiting from the capital, Yaoundé. Among them was Dr Nkwescheu Armand from the Direction of operational research at the Ministry of Health. I also had the opportunity to listen to typical Cameroonian music—makossa.

The following day Professor Luma and other colleagues took me on a tour to the slopes of Mount Cameroon (120 km away from Douala) and Professor Luma invited me to his beautiful family home. There I had the opportunity to meet his wife and the vice-Dean of the Faculty health sciences, university of Buea (UB), (Dr HE Gregory), Professor Roland Ndip the registrar of UB, and other colleagues from that institution.

Goal Summary 2015
- Continuing and further exploring the possibilities of the joint meetings and workshops to mutual benefit.

It included a talk on how to formulate a research question and hypothesis, as well as a talk on types of epidemiological studies and study design. Professor Henry Luma (Medical Director, Douala Hospital) gave an excellent talk on the opportunities and challenges of research at Douala General Hospital. The main theme of the day, Action for Clinical Research and Good Medical Practice, was highlighted by Professor Eugene Belley Priso (Director General of Douala General Hospital).

There are some important aspects which need to be formalized in order to do research, including the establishment of a formal Ethics Committee, implementation of a recognised Good Clinical Practice (GCP) course, as well as a dedicated programme for trainees to learn about research methodology. We have established that a partnership between Douala Hospital and the University of Cape Town would provide opportunities for collaborative research and student exchange.

Guidance on applications for funding would be also be an important element of such a research programme.

Visit to Douala General Hospital
I was thankful for the opportunity to visit this facility which serves a large community (2.1 million people) who live in Douala, which is the economical hub of Cameroon. The hospital has excellent facilities for renal dialysis (20 beds), a neonatal ICU, a well set-up maternity section and a dedicated cardiac department. The hospital is mainly open plan (see picture), which has advantages for infection control. Unfortunately, Cameroon has no
The Pulmonary Vascular Research Institute (PVRI) China Taskforce was established as a section of PVRI with the aim of exploring collaboration with doctors in China who have an interest in pulmonary vascular disease. PVRI China Task Force continues its active participation in organizing national pulmonary vascular meetings and education courses in China. During the last year, a number of meetings, social and research activities were held to Chinese physicians and scientists on the pathology, clinical presentation and management of PE and PH. Every opportunity was made to engage external speakers and create future international collaboration opportunities. PVRI-China Taskforce with the help of Chinese Medical Society (CMA) and the Chinese Thoracic Society (CTS) enabled a number of activities.

Educational events/meetings
- May 5th, 2014: World Pulmonary Hypertension Day. A series of educational and social activities for pulmonary hypertension were held in Beijing with the support of the I-seek pulmonary hypertension advisory group. More than 200 multidisciplinary physicians participated in the activities. The issues of health education, social support, medical insurance and standardize treatment for Chinese pulmonary hypertension patients were discussed.
- Sep 15th-18th 2014: The 14th National Conference of Chinese Thoracic Society was held in Zhengzhou, China. This meeting provided a communication stage that would ensure further progress in the epidemiology, diagnosis and treatment of pulmonary vascular disease including pulmonary embolism and pulmonary hypertension for physicians, scientists and other health care providers in China. Prof Davidson from, Bruce Davidson, from University of Washington School of Medicine talked about Thrombolysis of Pulmonary Embolism, State of the Art, 2014. A thoroughly discussion of the indications, dosages and regimens of pulmonary embolism was held during the meeting.
- August 2014: China Heart Congress. The one day and half pulmonary vascular disease session was attended mostly by cardiology physicians. Professors Martin Wilkins, Jason Yuan, Xiansheng Chen, Jianguo He, Lan Zhao, Zhen-guo Zhai gave lectures in the meeting, covering topics in advances in PAH, as well as in congenital heart disease and medical and surgical treatment of chronic thromboembolic pulmonary hypertension.
- Aug 2nd - 8th May 2014: Prof Michael Madani visited Beijing Chao Yang Hospital, Beijing Institute of Respiratory Medicine, to evaluate the operability for chronic thromboembolic pulmonary hypertension (CTEPH) patients. A half day symposium on CTEPH and PAH was held in Beijing Chao Yang Hospital. Prof Michael Madani, and his assistant gave talks covering the diagnosis, image evaluation, medical and surgical management of CTEPH. A US-China collaboration Center of Pulmonary Endarterectomy was also setup.
- July 12th-14th and Oct 29th -31st 2014: Two education courses on standardizing the diagnosis and treatment of pulmonary embolism and pulmonary hypertension were organized. These courses provided updates on several important aspects including diagnosis and treatment of acute pulmonary embolism and pulmonary hypertension, diagnosis technology, and standard thrombolytic and anticoagulant therapy, and clarified a standardized operational procedure for imaging pulmonary hypertension. These two courses brought some most recent points from the ESC 2014 pulmonary embolism guidelines and ACCP pulmonary hypertension guidelines. The courses provided an excellent learning and communication platform for physicians.

Publications


**Goal Summary 2015**

- Organise and facilitate the 8th PVRI Annual World Congress in Guangzhou, China, with the Chinese Medical Association and Chinese Thoracic Society.
to organize specific research programs. Much has been done to achieve these goals in 2014, with enormous collaboration of colleagues and professors from many countries around the world. Nonetheless, we still have a long way ahead, with open opportunities for participation of new members.

Educational activities
Published consensus

This is the final result of a series of discussions that were started in 2013, during the PVRI Annual Meeting in Istanbul, Turkey, with closing remarks in the Annual Meeting of 2014 (Bad Nauheim, Germany). The consensus covers several items related to the management of pediatric patients with severe pulmonary vasculopathy in a 1.5 year-old boy with non-restrictive VSDs and hypoplastic left lung, subjected successfully to repair after drug therapy for pulmonary hypertension. Pulmonary vascular resistance index was 9.5 units•m2 and 3.9 units•m2 respectively before surgery and six months after. Vertical and horizontal arrows indicate medial hypertrophy and severe intimal proliferation respectively. (Courtesy of Prof. Vera D. Aiello, Heart Institute, São Paulo, Brazil).
has been possible to reduce the frequency of severe postoperative complications to less than 10%. The study also includes biochemical and genetic determinations in this patient population. Based on the preliminary results, opportunities are open for new studies and sub-studies, and all collaborations are welcome.

**Goal Summary 2015**

New tasks and projects will be implemented in the Task Force in the years to come, with some of the new objectives as follows:

1. To develop guidelines for the management of adults with atrial septal defects.
2. To develop guidelines specific for the management of patients with Eisenmenger syndrome (all ages).
3. To organize studies for genotype and phenotype characterization of patients with congenital heart defects (and pulmonary hypertension) at all ages. Based on the preliminary results, opportunities are open for new studies and sub-studies, and all collaborations are welcome.

**PVRI Pulmonary Hypertension Associated with HIV Task Force**

**Task Force Leaders**
Nicola Petrosillo, Italy  
Sharilyn Almodovar, USA  
Sonia C. Flores, USA

**Task Force Members**
Rosie Burton, South Africa  
Anastase Dzudie, Cameroon  
Harrison Farber, USA  
Amam Mbakwem, Nigeria  
Okechukwu Ogah, Nigeria  
Jurgen Rockstroh, Germany  
Mahmoud Sanim, Nigeria  
Friedrich Thienemann, South Africa

**Publications**

**Research activities**
The HIV-PH Task Force is studying the viral evolution in HIV-infected individuals with pulmonary hypertension. We continue working on the development of molecular tools to gain more insights into the pathogenesis of HIV in PH. The lab is testing the nef and envelope isolates from HIV-infected patients and studying the impact of the coded HIV proteins in the biology of lung endothelial cells.

**Goal Summary 2015**

1. To increase the awareness of PH among the HIV specialists. We have implemented a short questionnaire to collect information about the current knowledge of HIV-PH among PVRI meeting attendees.
2. To support the enrollment of additional patients to the Latium Registry of PH.
3. Find a biomarker of PH that is low-priced, stable, and easy to use.
PVRI Schistosomiasis Task Force

**Task Force Leaders**
Rubin Tuder, USA  
Brian Graham, USA  
Rahul Kumar, India  

**Task Force Members**
Vera Aiello, Brazil  
Angela Bandeira, Brazil  
Ana Lucia Coutinho, Brazil  
Alexi Crosby, UK  
David Dunne, USA  
Allan Fennick, UK  
Rita Ferreira, Brazil  
Flavio Gapiassu, Brazil  
Ewa Kolosionek, Sweden  
Roberto Lambertucci, Brazil  
David Rollison, UK  
Russel Stothard, UK  

**Research activities**
We are continuing to investigate the pathogenic mechanisms by which inflammation results in pulmonary hypertension, primarily utilizing the Schistosoma-PH mouse model. The areas of active ongoing research are in the IL-4, IL-6, IL-13, and TGF-beta signaling pathways. We are collaborating with Dr. Angela Bandeira (Recife, Brazil) and Dr. Thais Mauad (Sao Paulo, Brazil) to obtain and characterize pulmonary tissue from individuals who died of schistosomiasis-associated PAH. We have received recent grant funding from the American Thoracic Society Foundation / Pulmonary Hypertension Association, American Physiological Society, National Institutes of Health, University of Colorado Department of Medicine, Gilead and Novartis to support our research.

**Goal Summary 2015**
1. We will continue our studies of the signaling pathways above, and plan to publish several manuscripts detailing our findings.

PVRI Exercise in Pulmonary Hypertension Task Force

**Task Force Members**
Ross Arena, USA  
Abraham Samuel Babu, India  
Bart Boerrigter, The Netherlands  
Marco Guazzi, Italy  
Bradley A. Maron, USA  
Jonathan Myers, USA  
Robert Naeije, Belgium  
Ron Oudiz, USA  
David Systrom, USA  
Aaron Waxman, USA  

**Initiatives**
The PVRI Exercise in PH Task Force continues to develop the documents proposed at the PVRI meeting in Germany in January 2014 that aim to address various aspects of pulmonary vascular and right ventricular function during exercise. A priority of the Task Force is to develop a standardized definition of exercise-induced pulmonary hypertension that is based on the totality of empiric evidence as well as expert consensus opinion. The Task Force members in charge of assembling this project include Abraham Babu, Ghazwan Butrous, Bradley Maron, Alexander Opotowsky, Robert Naeije, Aaron Waxman, John Ryan and David Systrom. A preliminary draft of the document is anticipated to circulate between Task Force members and will include novel clinical data intended to clarify some existing ambiguity regarding the appropriate metrics required to identify abnormal pulmonary vascular function provoked by exercise.

**Goal Summary 2015**
1. Guidelines statements on the benefits and limitations of exercise as a therapy in pulmonary vascular disease patients  
2. A call to action for new experimental laboratory models of exercise-induced pulmonary vascular dysfunction.
PVRI CHRONICLE: Volume 2 Issue 1, January - June 2015

PVRI WOMEN’S HEALTH & PREGNANCY IN PULMONARY HYPERTENSION TASK FORCE

Task Force Leader
Anna Hemnes, USA

Task Force Members
Barbara Cockrill, USA
Manal Al Hazmi, Saudi Arabia
David Kiely, UK
Timothy Lahm, USA
Mandy MacLean, USA
Ioana Preston, USA
Zeenat Safdar, USA
Victoria Wilson, UK

Publications
We have submitted our manuscript of guidelines for management of pulmonary hypertension and pregnancy for review at Pulmonary Circulation on September 10, 2014. We are waiting to hear back from reviewers presently.

Educational activities
We had a well attended session during the PVRI annual meeting in Giessen January 2014

Goal Summary 2015
1. Publish our guidelines for pregnancy in PH
2. Convene as a group to decide on next steps forward, likely via teleconference
3. Consider statement on hormone replacement therapy, other issues specific to women
4. Determine if additional PVRI members would like to join the group

Task Force Leader
Anna Hemnes, USA

Task Force Members
Barbara Cockrill, USA
Manal Al Hazmi, Saudi Arabia
David Kiely, UK
Timothy Lahm, USA
Mandy MacLean, USA
Ioana Preston, USA
Zeenat Safdar, USA
Victoria Wilson, UK

Publications
We have submitted our manuscript of guidelines for management of pulmonary hypertension and pregnancy for review at Pulmonary Circulation on September 10, 2014. We are waiting to hear back from reviewers presently.

Educational activities
We had a well attended session during the PVRI annual meeting in Giessen January 2014

Goal Summary 2015
1. Publish our guidelines for pregnancy in PH
2. Convene as a group to decide on next steps forward, likely via teleconference
3. Consider statement on hormone replacement therapy, other issues specific to women
4. Determine if additional PVRI members would like to join the group

PVRI PAEDIATRIC TASK FORCE

Task Force Leaders
Maria Jesus del Cerro, Spain

Task Force Members
Gabriel Diaz, Colombia
Sheila G. Haworth, UK
Antonio Augusto Lopes, Brazil
Liliana Moreno, USA
Usha Raj, USA
Julio Sandoval, Mexico

Educational events/meetings
1. January 2014: PVRI annual meeting (Giessen, Germany) 1
   • Pulmonary hypertension in children
   • The lung vasculature in bronchopulmonary dysplasia
   • Pulmonary hypertension classification in children post-Panama and Nice
   • Current and future therapy of pulmonary hypertension in children
2. February 2014: First Latin-American symposium on Pulmonary Hypertension in Children, Cartagena de Indias, 21-22 February 2014. Organized by PVRI (Dr. Gabriel Diaz) and Colombian Society for Cardiology and Cardiovascular Surgery
3. March 2014: 7th International Conference on Neonatal & Childhood Pulmonary Vascular Disease, organized by Drs. Ian Adatia, Jeff Fineman, and the UCSF.
4. September 2014: During the XV Latin Society for Pediatric Cardiology and cardiovascular pediatric Surgery meeting, a round table on pediatric pulmonary hypertension was held, with the participation of some members of the PVRI pediatric Task Force (Drs Gabriel Diaz, Lina Caicedo, and Maria Jesus del Cerro).

Other initiatives
After the roundtable, a meeting was held between these PVRI fellows and representatives of the Spanish and European Association for Pulmonary Hypertension, in order to organize the Colombian registry for pediatric pulmonary hypertension, in collaboration with the Spanish registry for pediatric pulmonary hypertension (REHIPED). As a result of this meeting, Drs. Caicedo and Gabriel Diaz held a meeting in Bogotá (8th November 2014), with Colombian pediatric cardiologist and neumonomists and Dr. Maria Jesus del Cerro (representing the Spanish registry) in order to promote the establishment of the Colombian registry.

Goal Summary 2015
1. Further development of the Latin-American symposium on Pulmonary Hypertension in Children
**Task Force Leaders**

Qadar Pasha, India  
Max Gassmann, Switzerland

**Task Force Members**

Serge Adnot, France  
Almaz Aldashev, Kyrgyzstan  
Inder Anand, USA  
Ghazwan Butrous, UK  
Paul Corris, UK  
Sheila G. Haworth, UK  
Alexandra Heath, Bolivia  
Friedrich Grimminger, Germany  
Ghulam Mohammad, India  
Robert Naeije, Belgium  
John Newman, USA  
Louise Ostergaard, Switzerland  
Nanduri Prabhakar, USA  
Ioana Preston, USA  
Kurt Stenmark, USA  
Patricia Thistlethwaite, USA  
Ishizaki Takeshi, Japan  
Jun Wang, China  
E. Kenneth Weir, USA  
Norbert Weissmann, Germany

**Educational events/meetings**

- Organised the 3rd International Leh Symposium ‘Ventilation and circulation in hypoxia: from mechanisms to patients and back’, 19-23 September 2014, in Leh, Ladakh, India
- Three bioscience graduate students were inducted for their course/dissertation in Dr. Qadar Pasha’s lab at IGIB
- One student of ‘Doctorate of Medicine’ was inducted for his degree course dissertation in Dr. Qadar Pasha’s lab at IGIB

**Research activities**

- Continuing from the 2013 research project entitled ‘Telomeres in Adaptation and Maladaptation Under Hypobaric Hypoxia’, a related project named ‘Telomere under hypobaric hypoxia’ has been introduced as a PhD program in Dr. Qadar Pasha’s lab.
- A research activity has been initiated on ‘the genetic comparison between the Indian and Bolivian patients of pulmonary hypertension’.

---

The climbers of the Stok Kangri
- Professor Alexandra Heath from Bolivia is the collaborator.
- A study on HAPH is being initiated with Prof. Talant Sooronbaev from Kyrgyzstan.

**Publications**

- Qadar Pasha. Saudi Guidelines on the Diagnosis and Treatment of Pulmonary Hypertension: Genetics of pulmonary hypertension” has been published in “Annals of Thoracic Medicine”

**Other initiatives**


**Goal Summary 2015**

1. The 7th National Leh symposium 2015 will be organized by NM hospital, Leh, Ladakh, Jammu & Kashmir, India after mid September 2015
2. Research activities in the above mentioned projects will be continued

---

**Task Force YOUNG COUNCIL Task Force**

**Task Force Leaders**

- Zeenat Safdar, USA
- Stylianos Orfanos, Greece

**Task Force Members**

- Elie El Agha, Germany
- Mrigendra Bastola, USA
- Mario Boehm, Germany
- Kzito Bwire, Kenya
- Guo Chen, China
- Mohamad Taha, Canada
- Salina Gairhe, USA
- Jose Gomez-Arroyo, USA
- Sachindra Joshi, USA
- Ewa Kolosionek, Sweden
- Djuro Kosanovic, Germany
- Nikki Krol, UK
- Ying-Ju Lai, Taiwan
- Ekaterina Legchenko, Germany
- Xiao-Hui Li, China
- Himal Luitel, Germany
- Gerald Maarman, South Africa
- Mamotabo Matshela, USA
- Alexander Opotowsky, USA
- Louise Ostergaard, Switzerland
- Oleg Pak, Germany
- Soni Pullamsetti, Germany
- Michiel de Raaf, The Netherlands
- Michael Seimetz, Germany
- Natascha Sommer, Germany
- Thenappan Thenappan, USA
- Michael Seimetz, Germany
- Michele de Raaf, The Netherlands
- Michael Seimetz, Germany
- Mariella Velez-Martinez, USA
Initiatives
The PVRI Young Council has continued to go from strength to strength throughout the year, and has increased membership to 30 members by December 2014.

- New Members
  The following new members have been recruited to the Young Council:
  - Elie el Agha
  - Florian Veit
  - Oleg Pak
  - Natascha Sommer
  - Himal Luitel
  - Mario Boehm

- Annual Points System
  During the year, the Young Council has implemented a ‘rewards based points system’ for all its members. Those who engage actively in the Young Council’s work, earn points throughout the year. At the end of the year, points can be redeemed against travel grants from the PVRI to the Annual World Congress on PVD or the Annual PVRI Drug & Discovery Meeting. Points are awarded for activities such as recordings for the educational website or actively contributing to the PVRI Chronicle. The most active members of the Young Council during 2014 have been Michael Seimetz and Djuro Kosanovic, both from the Giessen ECCPS group. Congratulations to both for their active engagement and great achievement. Congratulations are also in order for Young Council member Michiel de Raaf, who was elected Secretary to the Task Force and has created the Annual Points System.

Educational meeting/events
The Young Council met in person on a number of occasions, including during the following meetings:

  - The 8th PVRI Annual General Meeting and 7th Scientific Workshop & Debates, in Bad Nauheim and Giessen, Germany, 27-31 January 2014. During this meeting, the Young Council recorded numerous content for the PVRI educational website.
  - Young Council members were responsible for organising the PVRI Annual Get-Together during the American Thoracic Society meeting, 19 May 2014. A number of Young Council members also met to discuss the progress of the Council itself and the table of contents for the

Publications
- Vol 1 Issue 1 Chronicle
- Vol 1 Issue 2 Chronicle

Goal Summary for 2015
- Re-name the Young Council to ‘PVRI Committee for Young Clinicians & Scientists’ with direct reporting lines into the PVRI Executive Committee.
- Set up an executive structure and guiding document within the Committee incorporating roles such as President, Vice-President and Secretary and defining their roles and responsibilities.
- Set up effective communications lines with the PVRI Executive Committee to ensure members’ views are being represented at PVRI Executive and Board level.
- Expand and increase participation in the Annual Points System and administer PVRI travel grants which are awarded to members throughout the year.
- Publish the PVRI Chronicle twice a year.
our 312 published articles have been downloaded as PDFs over 64,000 times. Our top 35 most-accessed articles published in the two years 2013–2014 have been accessed via the UCP site alone over 23,300 times. The overall online usage of Pulmonary Circulation is up in the second half of 2014, with average access of PDF articles at 1344 per month, up from an average of 697 per month in the first half of the year, an increase of almost 52%.

**Promotion**
Pulmonary Circulation has continued its various promotional email blasts, and is continuing to grow our mailing lists. In the next year the PC office is reviving the newsletter and will be providing quality content in the form of Journal Office News, Spotlights, New Directions in Research, and Current Topics articles, as well as exciting articles from Young Scientists fresh from the front lines of research work. The office is developing a social media presence for the journal and increasing its visibility on various platforms. Additionally, Pulmonary Circulation continued to promote the journal at various international conferences, including the American Thoracic Society International Conference 2014, the American Heart Association Scientific Sessions, and the 7th Pulmonary Vascular Research Institute Scientific Workshops and Debates.

**Goals Summary 2015**
- In order to continue to provide open access to

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>Full-text HTML</td>
<td>Full-text PDF</td>
<td>Total</td>
</tr>
<tr>
<td>1</td>
<td>8445</td>
<td>1191</td>
<td>9636</td>
</tr>
<tr>
<td>2</td>
<td>8466</td>
<td>1140</td>
<td>9606</td>
</tr>
<tr>
<td>3</td>
<td>24141</td>
<td>4326</td>
<td>28467</td>
</tr>
<tr>
<td>4</td>
<td>25688</td>
<td>4325</td>
<td>30013</td>
</tr>
</tbody>
</table>
our articles and defray costs from our readers, *Pulmonary Circulation* will institute a publication fee in 2015. We want to keep this fee as low as possible and we are establishing funds to offset charges for authors from developing nations.

- *Pulmonary Circulation* has plans to re-launch our website with new and exciting features for our readers at www.pulmonarycirculation.org.
- Continue to broaden our readership. With the institution of social media channels and the re-launch of our website, we will continue to expand our audience and reputation.
- Increase citations made to the Journal. In an effort to ensure an acceptable impact factor for *Pulmonary Circulation*, one of our continuing main goals is to increase citations to PC.
- Articles posted online immediately after acceptance. With *Pulmonary Circulation*’s new publisher, we now have the option to post articles online immediately after acceptance for viewing by the general audience.
- Quicker acceptance to publication date. Our acceptance to publication date goal for 2015 is eight weeks from acceptance of the manuscript to Ahead of Print publication of the final article.

### Statistics

N=312 articles

**Pulm Circ, Types of Articles Published**

- Editorials – (29) 9%
- Review – (85) 27%
- Original Research – (143) 46%
- Guidelines & Other – (31) 10%
- Case Reports – (24) 8%

---

**Top 5 most downloaded articles published in 2014:**

<table>
<thead>
<tr>
<th>#</th>
<th>Title</th>
<th>Volume, Issue</th>
<th># accesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.</td>
<td>Repair of congenital heart disease with associated pulmonary hypertension in children: what are the minimal investigative procedures? Consensus statement from the Congenital Heart Disease and Pediatric Task Forces, Pulmonary Vascular Research Institute (PVRI), Antonio Augusto Lopes, Robyn J. Barst, Sheila Glennis Haworth, Marlene Rabinovitch, Maha Al Dabbagh, Maria Jesus del Cerro, Dunbar Ivy, Tarek Kashour, Krishna Kumar, S. Harikrishnan, Michele D’Alto, Ana Maria Thomaz, Leina Zorzanelii, Vera D. Aiello, Ana Olga Mocumbi, Maria Virginia T. Santana, Ahmed Nasser Galal, Hanaa Banjar, Omar Tamimi, Alexandra Heath, Patricia C. Flores, Gabriel Diaz, Julio Sandoval, Shyam Kothari, Shahin Moledina, Rlivani C. Gonçalves, Alessandra C. Barreto, Maria Angélica Binotto, Margarida Maia, Fahad Al Habshan, and Ian Adatia</td>
<td>Vol. 4, No. 2</td>
<td>1260</td>
</tr>
</tbody>
</table>
PVRI Chronicle

Editor-in-Chief
Sachindra Joshi, USA

Executive Editor
Nikki Krol, UK

Initiatives
The PVRI Chronicle was launched in January 2014 as a bi-annual non peer-reviewed journal. Initiated by the PVRI Young Council, the journal includes interactive discussions on controversial questions as well as case reports and research from all over the world. As of December 2014, the PVRI Chronicle has an official ISSN number and is registered with the British Library UK.

In the latest issue, the PVRI Chronicle has a patient-oriented slant, including a report from the Head of the Greek pulmonary hypertension patients and caregivers, the Hellenic Pulmonary Hypertension (H.P.H).

This embodies the spirit and flavour of the PVRI Chronicle: to be a brand ambassador of the PVRI by upholding the Institute’s mission statement regarding research, education and clinical care, but also to include all those affected by pulmonary vascular disease (PVD), be they doctors, clinicians, researchers, or patients. Pulmonary vascular disease affects us all, and must be dealt with by us all.

Publications
To this end, PVRI Chronicle aimed to publish the first issue in January 2014, with the second following in July 2014. The second issue was delayed slightly to ensure a quality publication, and has been online since August 2014.

- PVRI Chronicle Volume 1 Issue 1: This issue was well received by the membership in online only format. Packed full of information and links, the editorial board received overall excellent feedback. This first issue of the journal spanned 95 pages.
- PVRI Chronicle Volume 1 Issue 2: Published online only in August 2014, this issue included a wide variety of topics including exercise-induced pulmonary hypertension, pregnancy and pulmonary vascular disease, chronic obstructive pulmonary hypertension (COPD), and a number of meeting reports. Many of the articles contained active links to educational material on the PVRI website. This issue was 72 pages.

The covers of the issues for PVRI Chronicle Volume 1
For 2015, PVRI Chronicle again plans two issues. Volume 2 Issue 1 will be the journal’s first print issue, although all issues remain available for print on demand. The January-June 2015 journal will be available at the 8th PVRI Annual World Congress in Guangzhou, and will contain the scientific agenda and the PVRI Annual Report, as well as original articles on anti-oxidants in COPD, a commentary of pulmonary hypertension in the developing world, and a unique take on the discovery of the pulmonary circulation, totalling 95 pages.

Further initiatives
- The plans for a PVRI app, and therefore a PVRI Chronicle app, are currently stalled. However, PVRI Chronicle seeks to further explore the possibilities of publishing in app format for implementation in 2016.
- PVRI Chronicle seeks to expand their pool of submissions, and does so by inviting potential authors to contribute in person to adminpvri@gmail.com. Similarly, the Editorial Board is employing social media to increase awareness and readership of the journal, and so further encourage submissions.

Goal Summary 2015
- Continue to publish engaging, encompassing features.
- Publish on time every time.
- Further explore the possibilities of publication in app format for iPhone and iPad.
- Expand the readership.
- Expand the submission pool.
Overview of 2014

PVRI Staff
PVRI welcomed two new members of staff during the year. On 1 April 2014 Stephanie Barwick started her official employment as Executive Director with the PVRI. Stephanie is the first full-time employed Chief Executive of the PVRI and she is based in the UK Central Office in Canterbury, Kent working with Nikki Krol, Executive Administrator. The second new member of staff the PVRI welcomed during the year is Annisa Westcott, who replaced Christina Holt as Managing Editor for Pulmonary Circulation in June 2014. Annisa is based with Dr Jason Yuan, Chief Editor of PC, in Tucson, USA.

PVRI Board of Directors and Advisors
The PVRI BODA saw a number of changes in 2014. Professor Sheila G. Haworth replaced Professor Martin Wilkins as PVRI President, and Dr Stuart Rich as the Chairman of the Board. In spring this year, Professor Ghazwan Butrous stepped down as Managing Director, and was awarded the honorary and well-deserved title of ‘PVRI President Emeritus’. Board member Professor Julia Polak sadly passed away after a long battle with pulmonary vascular disease. Her obituary is available on the PVRI website.

PVRI Membership
The PVRI membership has increased to a total of 760 members. The PVRI is a true global charity reaching out to over 60 different countries in the world, where its members are based.

PVRI Annual Dues
The PVRI conducted a membership analysis in May 2014. Due to a large percentage of members/fellows who had not paid their annual dues, an intensive campaign to chase up outstanding membership subscriptions was conducted sending personalised emails to every member who had not paid their fees, as well as follow-up phone-calls to members in countries where the economic climate was such that no excuse for non-payment could be made. Of the countries targeted, only 54% had paid their membership pre-phone calls. Immediately post-phone calls, the percentage had risen to 63%. By the end of July, the number of paying members from targeted countries rose to 73%. Overall, the phone calls caused a rise of 19% of paying members in targeted countries. In 2015 members and fellows who have not paid or renewed their membership dues will no longer have access to a reduced registration fee to the PVRI scientific meetings, nor access to the PVRI educational website.

PVRI Registration Fees to Scientific Meetings
At the last AGM in Giessen, Germany, the Board decided that registration fees to its scientific meetings had to be introduced to PVRI members/fellows, albeit at an extremely reduced rate. This was necessary in order to ensure the PVRI’s long-term financial sustainability. The registration fee for PVRI members and fellows was set at $150.

PVRI Constitution
In order to reflect the new structure of the PVRI with its recruitment of an Executive Director, internal management structures needed to be clarified and defined which resulted in a new PVRI constitution which has been devised. The constitution outlines the PVRI’s internal governance and management structure. The new constitution will be presented to all members at the AGM in January 2015 and, once ratified, made available to all members and fellows via the PVRI website.

PVRI Marketing
A new PVRI brochure was designed which gives information on the charity to potential new members. It details past achievements and successes and gives information on membership benefits. In addition to the brochure, regular monthly online newsletters have been designed and sent to all members highlighting specific meetings or important aspects of the Charity. In 2015 it is intended to update the current PVRI logo and website to give a more corporate image and consistent brand.

PVRI Strategic Report
A Strategic Report 2015-2018 has been produced which outlines the Charity’s goals for the next three years. The plan gives a brief history of the PVRI as well as highlights the PVRI’s values, aims and objectives. It is used in communication with members
As well as for future fundraising purposes.

PVRI Social Media
January 2014 saw an initial surge in the PVRI Social Media, which translated to 68 ‘likes’ on the PVRI Facebook page. Since September 2014, Executive Administrator Nikki Krol has taken on the role of Social Media Manager and has significantly increased outreach on Twitter, Facebook and more recently, LinkedIn. Compared to November 2013, the Facebook page has increased its ‘likes’ nearly 300% to 190 ‘likes’ as of printing. Additionally, the social media reach has also risen, and posts now average 750-1000 views per week. Although these numbers are promising and bound to increase further in 2015, PVRI appeals to its membership to help spread this message of awareness, research and education further via the social media. A powerful and far-reaching tool, a ‘like’ or ‘share’ brings pulmonary vascular disease awareness right into the reader’s home, workplace and cellphone. To this end, PVRI encourages the membership - all 760 individuals - to find the Pulmonary Vascular Research Institute page on Facebook and to ‘like’ and ‘share’ it with colleagues, family and friends. PVRI aims for #760LikesIn2015.

New PVRI Task Force
A new PVRI Task Force in Central Asia comprises the countries of Kazakhstan, Kyrgyzstan, Uzbekistan, Tajikistan, Turkmenistan and Mongolia. They held their first meeting in June 2014 in Kyrgyzstan, attended by PVRI President Sheila Glennis Haworth and Executive Director Stephanie Barwick amongst others. The meeting was a great success and plans are now underway for the next Scientific Meeting in April 2015 in Kazakhstan.

New PVRI Drug & Development Symposium
In June 2014, the first PVRI Drug Discovery & Development Symposium in conjunction with the FDA (Food & Drug Administration USA) was held in Bethesda, USA. Approximately 100 delegates attended the meeting. The next meeting of this kind will be held in Jun 2015 in London, UK.

New Online Course on PVD
The PVRI is currently in the process of conducting a feasibility study into the viability of developing an online course on PVD. Conversations are being held with Cambridge University in the UK who are interested in potentially hosting such a course. The results will be published to all members/fellows in March 2015 together with a plan how best to implement the findings of the report and take the idea forward to the next stage.

PVRI Fundraising
Fundraising activities have commenced in 2014 and will become an important element of the PVRI’s work in the future, not only to sustain the PVRI’s long-term financial future, but also to promote PVD and raise awareness about the disease and highlight the valuable work of the Charity. In 2014 PVRI Executive Administrator Nikki Krol organised a Spartan Fundraising Challenge which involved conquering a gruelling 21km obstacle course, which included mud crawls and fire jumps. Together with eight friends and colleagues, Nikki raised an impressive $3155, 126% of the original goal. The next fundraising event is planned on 5th May 2015 to celebrate ‘Global Pulmonary Hypertension Awareness Day’ in the form of a charity concert which will be held in Canterbury, UK together with the Festival Chamber Orchestra.

Collaboration with Other Societies
The PVRI has collaborated with a wide range of PVD related societies and organisations, e.g. the International Society for Heart & Lung Transplantation (ISHLT), the Pulmonary Hypertension Association (PHA) in the UK and USA, the American Heart Association (AHA) as well as many other important stakeholders in PVD. The PVRI anticipates further collaboration with likeminded organisations across the world in order to increase the PVRI’s mission of raising awareness on PVD and highlight the work of the Charity.

Sponsorship & Funding Received
We are grateful to Bayer Pharmaceutical AG, Gilead and Glaxo-Smith-Klein who have all participated in our Roundtable membership in 2014 and provided important sponsorship to the PVRI which has allowed us to implement our mission and goals for the year. In addition to the pharmaceutical donations, we have received funding from the Cardiovascular Medical Research & Development Fund (CMREF) which has allowed us to organise the first PVRI Drug Discovery & Development Symposium in Bethesda, USA, in July 2014, conduct a feasibility study into the viability of an online course on PVD and employ a full-time Executive Director.

PVRI Chronicle: Volume 2 Issue 1, January - June 2015
An Introduction From the New PVRI Chief Executive Stephanie Barwick

My first nine months with the PVRI have been a journey of excitement, reflection and discovery. I was fortunate to get a glimpse of the ‘PVRI in action’ before I started my official employment on 1st April 2014, as I attended the 8th PVRI Annual General Meeting and 7th Scientific Debates and Workshops, which was held in Giessen, Germany in January 2014. During this event, I had the opportunity to meet members of the Board of Directors as well as many PVRI members and fellows from across the world. This experience was truly invaluable as it provided me with a real understanding of the PVRI’s mission and what it actually means to be a truly global charity working with so many like-minded, yet different people from across the world. I do not think that I could have been more inspired to start my job with such a good foundation and introduction than to experience first-hand the PVRI’s mission, membership and challenges during this scientific meeting.

When I then started my role on 1st April 2014, I was very excited to take on this challenge and meet even more of our members experiencing their work in their own countries. In May 2014, I participated in the SAPH meeting which was held in the Oman, followed by a visit to Kyrgyzstan in June 2014 to attend the first scientific meeting of our newly established Task Force in Central Asia. In July, I participated in my first PVRI Board of Directors meeting in Bethesda, USA, which was held during the first PVRI Drug Discovery & Development Symposium. Alongside being greeted with the most hospital welcome by our members in these wonderful countries, back in the office, I have worked on establishing the new PVRI regulations which set out our internal governance and management structures, I started to implement improved internal operational procedures, submitted new funding proposals and compiled end of year reports for existing funders, liaised with various sponsors from the pharmaceutical industry on annual donations, set out a social media strategy, worked with the members of the Young Council on implementing a reward based membership scheme, developed various new marketing materials and, of course, helped to organise the 8th PVRI Annual World Congress in Guangzhou, China. None of this, I may add, would have been possible without the help of Nikki Krol, the PVRI Executive Administrator, who has been a huge support to me. Her inside knowledge of the PVRI is invaluable and she has been an enormous asset to me during these first nine months. Thank you Nikki!

So, after all of the above, what’s my view of the PVRI now and what is the plan for the future? First of all, the good news is that I still think of the PVRI as an outstanding organisation with a true global focus and appeal. It is unique in the sense that it is the only global charity dedicated to raising awareness of PVD and it has attributed a membership consisting of some of the most renowned clinicians and scientists in their field. Our mission and work is invaluable and there are many examples of the value of what we do and how we have impacted on the world around us. We are an independent voice of authority with an excellent reputation.

However, in my opinion, the PVRI is at a crossroads from being a reasonably small, mainly volunteer-run organisation to becoming a professional company with longevity. Everything that has been achieved up until now has been as a result of the tireless work of some of our members. This is admirable, but not a sustainable plan for the future. Our challenge now is to build on what we have achieved, maintain the character and focus of the PVRI, but move the organisation into a more corporate structure, which is fit for growth in the future. This involves setting up certain internal processes and systems which include improved accounting and financial monitoring procedures, division of power and workload by setting up...
various sub-committees, future planning and goal setting, engaging in fundraising activities, collaborating with other like-minded societies and organisations across the world, identifying suitable funding avenues for particular projects and member-led activities, developing revenue streams from current activities to sustain our services for the future and last, but not least, putting in place measurements that allow us to monitor success and growth.

This is not easy and as with any organisation that moves from ‘good to great’, difficult decisions will have to be taken, which may not be popular. Increased internal expenditure on more consultancy and/or permanent staff needs to be considered to support and allow existing services to improve and grow and putting aside funding for new activities.

We have set out our goals for the future in our Strategic Plan which focuses on the next three years. This is an ambitious plan for the future and I hope that you will agree with the goals and targets we have set for ourselves. Your support and continued membership is of the utmost importance and I would like to express my personal thanks to you for your involvement in the PVRI. If you wish to become more active in the PVRI and get involved in some of our exciting activities in the future, please do not hesitate to get in touch. We value any support, help and engagement that you can offer and I promise you won’t be disappointed as we are embarking on an exciting journey ahead of us.

I would like to express my thanks to all our members who have made me feel so welcome during the past nine months, the members of the Board of Directors for their trust and confidence in me and, in particular, the President and Chair of the Board, Sheila Glennis Haworth, for her continued support and encouragement.

PVRI Staff 2014

A Brief Biography of the New Pulmonary Circulation Managing Editor Annisa Westcott

Annisa Westcott joined the quarterly peer-reviewed journal Pulmonary Circulation in July of 2014 as Managing Editor.

Annisa graduated Magna Cum Laude from the University of Arizona with dual B.A. degrees in Linguistics and English. She brings with her several years’ worth of editing experience, including five and a half years at an NSF-funded Science and Technology Center at the University of Arizona, where she edited scientific articles, book chapters, reports, and even a textbook. She also worked for more than two years as a freelance editor and has over a decade of experience in business administration.

Annisa’s interests are in digital publishing, branding, web development, platform-building, SEO, and social media. She is excited to be working as Managing Editor of Pulmonary Circulation and hopes to bring her interests and experience to bear in growing Pulmonary Circulation’s online presence and readership with an eye to the future. Her plans include re-developing the Pulmonary Circulation website and brand in order to make it the most looked-to resource for the latest information on pulmonary vascular disease research.

Annisa is also a prolific writer and poet, whose current works-in-progress include a three-volume sci-fi/urban fantasy series of novels and an anthology of related short stories.

Mrs. Annisa Westcott

Annisa is a native Tucsonan and is based in the Tucson office, working closely with Editors-in-Chief Jason Yuan and Nick Morrell.

Annisa is a foodie and is making it her mission in 2015 to introduce Dr. Yuan and the members of his lab to the local Tucson culinary scene.

Annisa is the main point of contact for all Pulmonary Circulation requirements. If you have questions or just wish to welcome her to the Journal, please don’t hesitate to contact her at annisa@email.arizona.edu.
Professor Ghazwan Butrous steps down as PVRI Managing Director

The PVRI would like to thank Professor Ghazwan Butrous for his outstanding contributions to the PVRI since its inception in 2006. Acting as PVRI Managing Director from its humble beginnings to spring 2014, Ghazwan was instrumental in the Charity’s growth and increase in membership from a small handful of dedicated founders to what is now the only global medical research charity with over 750 members in 60 different countries. His vision of the educational website and input to the Institute’s flagship journal Pulmonary Circulation as ‘Senior Editor’ has ensured the PVRI’s steady growth in size and reputation. At the January 2014 Board of Directors and Advisors meeting in GiesSEN, Germany, he was voted unanimously ‘President Emeritus’, a title he surely deserves.

Ghazwan has recently decided to step down from the PVRI Board of Directors, but will continue to play an active role in the PVRI in the future. Thank you Ghazwan for all your passion and tirelessly energy!

Professor Julia Polak, PVRI Board of Director Member, passes away

It is with very great sadness that we inform you of the death of Dame Professor Julia Polak, DBE. She passed away Monday 11th August. She was a member of the PVRI Board of Directors and a very valued contributor in the field of pathology and tissue engineering. She will be greatly missed.

“Who knows what will happen in five or ten years. There are lots of hurdles to overcome [but] creating an atmosphere of really multidisciplinary teams including everybody, including patients, to work together with companies and science: it needs work but it’s happening.”

- Dame Professor Julia Polak, DBE

Professor Martin Wilkins resigns as PVRI President and is replaced by Professor Sheila Haworth CBE

In December 2013, Professor Martin Wilkins officially resigned as PVRI President after completing his agreed term. Professor Wilkins served as PVRI President for three years, during which time membership increased significantly and the PVRI expanded its activities on a global scale. Professor Wilkins was replaced by Professor Sheila G. Haworth in January 2014, who was introduced during the Annual General Meeting and has been an active member of the PVRI Board of Directors for many years.

Who knows what will happen in five or ten years. There are lots of hurdles to overcome [but] creating an atmosphere of really multidisciplinary teams including everybody, including patients, to work together with companies and science: it needs work but it’s happening.”

- Dame Professor Julia Polak, DBE

“Who knows what will happen in five or ten years. There are lots of hurdles to overcome [but] creating an atmosphere of really multidisciplinary teams including everybody, including patients, to work together with companies and science: it needs work but it’s happening.”

- Dame Professor Julia Polak, DBE

Professor Martin Wilkins, Former PVRI President

Professor S. Haworth CBE, PVRI President
In September 2014, Executive Administrator Nikki Krol and Adam Lucas initiated a ‘Spartan Fundraiser’, which included 3 races, 8 people, and a fundraising goal of $2500 USD.

The PVRI Spartan Team was overwhelmed by the fantastic response to the PVRI Spartan Fundraiser initiative. Over the course of two months, three races, and a total of 39 km, donations from the PVRI membership saw the team surpass the original $2500 goal by 126% and raise $3155 for the PVRI.

Compared to previous fundraisers, such as the Amsterdam Half Marathon fundraising initiated by Nikki Krol in 2012 which raised just shy of $2000, the recent effort increased both funding and awareness. A big thank you from PVRI for all those who contributed to this effort.

To continue the momentum, PVRI is organizing a fundraising effort on 5 May 2015 for World Pulmonary Hypertension Day in the form of a Charity Concert in Kent, United Kingdom. More information can be found online, and tickets are now available via the Gulbenkian box office: https://uk.patronbase.com/ Gulbenkian/Sections/Choose?prod_id=PVM1&perf_id=1

---

The PVRI Spartan Team, detailing their motivation for running obstacle course races for PVRI.