

HYPERTENSION NEWS

September 2014, Opus 38



International
Society of
Hypertension

NOTES FROM THE EDITOR

Lars H. Lindholm

Dear ISH Member

Please find enclosed the September issue of Hypertension News (HT), Opus 38. I am afraid that this is a bit late. The reason for this is that many of us have been on vacation in August-September. Helen (Secretariat) has had to work harder than usual to collate the promised contributions.



Million thanks Helen and thanks also to all of you who have contributed! I would also like to thank Bo Carlberg, Umeå, Sweden who is leaving the HT News team as well as the ISH Executive and Council this autumn to dedicate more time to his research students.

Bo, you have contributed in an outstanding way and without your help the ISH newsletter would not be what it is today! The good news is that Bo has promised to continue to help us in the future in a more "freelance" way! Professor Thomas Kahan from the Karolinska in Stockholm has stepped in and will gradually take over Bo's work for HT News e.g. the HOT off the Press - Clinical section. I am sure that Thomas is known to most of you. He is an outstanding researcher with a special focus on "hypertension and the heart". Welcome Thomas!

In this issue of HT News the new President of ISH presents her views on the future and where she wants to take the Society. Exciting stuff!

Please join me in welcoming Rhian as the 1st female President of our Society.

Have a good read!

Lars H Lindholm, Editor

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FROM THE ISH PRESIDENT: VISION FOR THE ISH 2014-2016

Rhian Touyz



I am delighted to begin my tenure as President of ISH and am looking forward to working with the leadership in taking our Society forward over the next two years.

It is a pleasure to introduce the new Executive including:

Louise Burrell (Australia)	Treasurer & Corporate Liaison Officer
Masatsugu Horiuchi (Japan)	Secretary
Neil Poulter (UK)	Chair, Communications Committee
Dorairaj Prabhakaran (India)	Ex-Officio International Development Officer
Agustin Ramirez (Argentina)	Vice President
Ernesto Schiffrin (Canada)	Immediate Past President
Alta Schutte (South Africa)	Chair, Membership Committee & New Investigator Liaison Officer
Michael Weber (USA)	Officer at Large - Global Initiatives
Jiguang Wang (China)	Global Outreach & Promotion Officer

New Council members 2014-18 are listed on page 6.

As your President I will fulfill my mandate by ensuring the objectives of the Society are met in that I will work actively with the leadership to promote and encourage the advancement of scientific research and knowledge and its application to the prevention and management of heart disease and stroke in hypertension and related cardiovascular diseases around the world. In addition, I will develop new initiatives and fresh ideas with priority areas being:

1. Investing in the next generation of hypertension researchers through continued support of the New investigator Network and by creating new schemes to promote opportunities for networking, training, summer schools and funding, focusing on all regions and especially on those in the low income regions.
2. Establishing a 'Big brother mentoring scheme' for trainees and young researchers where junior researchers will be paired with more senior researchers.
3. Nurturing our future ISH leadership is essential and we will create a new category of membership through the 'Emerging Leaders' category. This category falls between 'research fellows' and 'regular members' and aims to provide a transition period from 'trainee' to 'professional member'. New awards and special benefits will be available to members in the 'Emerging Leaders' category.
4. Expanding the already very successful workshops in Africa and South America to Asia and Central America and to other less well-served regions. We will embed 'train the trainer' programs in such workshops and seminars.
5. Developing a programme to support and mentor women in hypertension research.
6. Promoting the ISH guidelines and developing teaching aids and slide sets that are region-appropriate.
7. Working with global leaders and national associations to promote outreach programmes to educate the public about hypertension and to have impact on hypertension awareness.

I am grateful to the immediate Past President Dr Schiffrin and his leadership team for passing on a Society with a strong trajectory of growth and excellence. Working together with the outstanding and energetic new ISH Executive and Council committees, with truly global representation, I look forward very much to an exciting and productive two years ahead.

Highlights to look forward to are the next ISH Scientific Meetings in Seoul 2016, Beijing 2018 and Glasgow in 2020, so please plan on attending these meetings and bring along your best research in hypertension as well as your colleagues and trainees. Also, the regular outstanding newsletter will provide you with up-to-date global hypertension-related activities and will keep you connected to colleagues.

Your leadership represents you, so if you have any comments, concerns or suggestions, please pass these onto us through Helen Horsfield, in the ISH Secretariat office (email secretariat@ish-world.com).

Rhian Touyz
President, ISH (2014-2016)

The TASMIN-SR Trial. The new way to treat hypertension

Bo
Carlberg

Umeå
University
Hospital

Umeå
Sweden



Traditionally, blood pressures are measured by a doctor or a nurse or at home by the patient or a relative. However, decisions about adding new drugs or increasing the doses, are most often done by a doctor.

For many years, many patients with insulin treated diabetes have been dosing their insulin from a synthesis of blood sugar levels, the forthcoming meal and physical activity. Could similar regimens be applied to the treatment of hypertension?

In a recent paper published in the Journal of the American Medical Association (JAMA), Richard McManus¹ et al present a randomized controlled trial where patient-controlled treatment of hypertension including self-monitoring and self-titration of antihypertensive drugs was compared with usual care. All patients in the study had high cardiovascular risk.

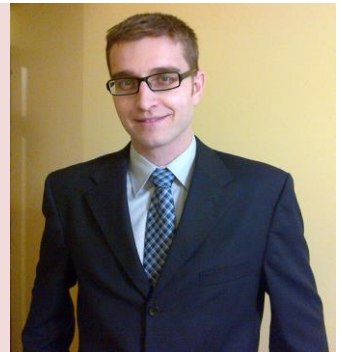
After 12 months, the patient-controlled group had 9.2/3.4 mm Hg lower blood pressure than what usual care achieved. This is a well-conducted study. However, the patients included in the study were highly selected and may not represent the usual patient.

If we put this in our daily routine, it is obvious that it has the potential of having huge impact on hypertension treatment and will make it possible for more patients to reach treatment goals. This is the beginning of a new way to treat hypertension and we have certainly only seen the beginning of a “bring it home blood pressure lowering strategy” as described in the accompanying editorial comment².

1. McManus RJ, Mant J, Haque S et.al. *Effect of Self-monitoring and Medication Self-titration on Systolic Blood Pressure in Hypertensive Patients at High Risk of Cardiovascular Disease.* JAMA 2014; 312:799-808.
2. Nilsson PM, Nyström FH. *Self-titration of Antihypertensive Therapy in High-Risk Patients.* JAMA 2014; 312:795-6.

A selective microRNA-based strategy inhibits restenosis while preserving endothelial function

Santulli G, Wronska A, Uryu K et al. *A selective microRNA-based strategy inhibits restenosis while preserving endothelial function.* J Clin Invest. 2014;124(9):4102-4114. doi:10.1172/JCI76069.



Dylan Burger

Communications
Committee &
NIC Member
Ottawa, Canada

This manuscript, published in the September issue of Journal of Clinical Investigation (JCI), is not directly related to hypertension but a common comorbidity.

As the incidence of coronary artery disease increases worldwide, so too does the need for revascularization through percutaneous coronary intervention (PCI). Most commonly, PCI procedures are coupled with the insertion of stents which provide a physical support for revascularization and dramatically reduce restenosis rates, particularly with drug-eluting stents which release antimitotic agents (i.e. sirolimus) that prevent smooth muscle cell proliferation. Indeed drug eluting stents are potent inhibitors of neointimal hyperplasia, the major cause of restenosis after angioplasty /stenting.

One problem with drug eluting stents is the lack of specificity of action. While they effectively inhibit smooth muscle cell proliferation they also inhibit re-endothelialization of the vessel and this may predispose to future thrombotic events. In a recent study from JCI, Santulli and colleagues employed a micro RNA (miRNA)-based approach to overcome this lack of selectivity. The authors generated a targeted adenovirus containing both a cyclin-dependent kinase inhibitor (p27^{kip}) to inhibit cell proliferation and target sequences for endothelial cell specific miRNA-126-3p which promotes angiogenesis. Using both cellular models and a rat balloon injury model the authors observed that this adenovirus (termed *Ad-p27-126TS*) blocks smooth muscle cell proliferation while preserving endothelial health and proliferation. Of particular interest was the observations in a rat arterial balloon injury model where administration of *Ad-p27-126TS* improved re-endothelialization from 23% to 80% as early as 2 weeks despite equivalent inhibition of neointimal hyperplasia. This study provides an exciting proof of concept for the selective inhibition of restenosis using a novel adenovirus approach.

Hypertension Research in Sapporo Medical University

Masato Furuhashi¹⁾, Kazuaki Shimamoto²⁾

1) Department of Cardiovascular, Renal and Metabolic Medicine, Sapporo Medical University School of Medicine

2) President, Sapporo Medical University



Kazuaki Shimamoto



Masato Furuhashi

Sapporo Medical University

Sapporo Medical University is a medical university in Hokkaido, the northernmost island of Japan. Founded in 1950, it has a history of more than 60 years. The university consists of the School of Medicine, the School of Health Sciences and the Center for Medical Education. All strive to enhance education, research, and medical care and contribute to medical services in Hokkaido, adhering to the following three principles: training medical professionals with a well-rounded character, improving medical services for the residents of Hokkaido and promoting advanced international research. In a long history of medical research, pioneering studies in Sapporo Medical University have been providing excellent results that reflect significant improvement in regeneration medicine for cerebral infarction and development of



Sapporo Medical University Hospital

cancer vaccines in Japan as well as hypertension-related research.

Sapporo Medical University Hospital as a medical institution attached to the university plays a central role in clinical education and research and produces excellent human resources through the education and training of medical staff and professionals with high levels of expertise. The hospital has facilities of 26 clinical divisions and 938 inpatient beds. It provides advanced, state-of-the-art medical care, such as emergency medical care, cancer treatment and regenerative medicine, and also plays a significant role as a medical institution that assists the development of local medical services and accepts patients from remote areas in Hokkaido in cases of disasters. The hospital also provides advanced medical treatment for various intractable diseases. A cancer vaccine therapy as a new approach to treatment and nerve regenerative medical techniques to repair cerebral infarctions and spinal cord injuries are among the medical practices based on original fundamental research that have attracted the attention of medical experts in Japan and abroad.

Department of Cardiovascular, Renal and Metabolic Medicine

The Department of Cardiovascular, Renal and Metabolic Medicine in Sapporo Medical University has been contributing to hypertension research in Japan. As an opinion leader, Dr. Shimamoto, the former Professor of the department, is currently the President of Sapporo Medical University and one of the most famous clinical hypertension researchers in Japan. He contributed to the International Society of Hypertension (ISH) as a council member (2006-2014). He was also a council member of the Japanese Society of Hypertension (JSH) and the President of the JSH (2008-2010) and held annual meeting of the JSH in 2008 in Sapporo. Additionally, he has just published the JSH guideline for the treatment of hypertension (JSH 2014) as a chairperson of the Committee.

In the department, we have been investigating cardiovascular, renal and metabolic diseases using methodologies of basic, clinical and epidemiological sciences. Studies on hypertension, myocardial protection, clinical cardiology and cardiovascular epidemiology are conducted by separate research groups, but many of the research projects involve inter-group collaboration as well as collaboration with investigators abroad.

The Hypertension Research group in the department has been focusing on mechanism of insulin resistance and pathophysiological roles of the renin-angiotensin system (RAS) and the kallikrein-kinin system (KKS). Since we showed that insulin resistance contributes to hypertension through sodium retention and augmented activation of sympathetic nerves and the RAS (Shimamoto K, et al. *Hypertension* 1994), we have mainly investigated mechanisms and outcomes of insulin resistance, such as down-regulation of GLUT4, reduction in insulin-sensitive type I skeletal myocytes, tissue specific impairment of insulin signaling and

inhibition of AMP-activated protein kinase-mediated pathway by angiotensin II. Furthermore, we have characterized relationships between angiotensin II type 1 receptor, ACE2 and angiotensin 1-7 in pathobiology of the RAS. Regarding the KKS, we demonstrated that the bradykinin B1 receptor plays important roles in protection of the kidney and heart from fibrosis and remodeling under hypertension.

Recently, we are interested in adipokines, bioactive molecules derived from adipocytes, in hypertension-related diseases. We previously demonstrated that adiponectin, an anti-diabetic and anti-atherogenic adipokine, is decreased in essential hypertensives and that RAS blockade increases adiponectin with improvement of insulin resistance for the first time (*Hypertension* 2003). In addition, we currently focus on another adipokine, fatty acid-binding protein 4 (FABP4). We and our collaborators previously demonstrated that FABP4 plays a significant role in many aspects of metabolic syndrome, including obesity, diabetes, and atherosclerosis (*J Clin Invest* 2008; *Nat Rev Drug Discov* 2008) and that a FABP4 specific inhibitor can treat diabetes and atherosclerosis in several animal models in a target specific manner (*Nature* 2007). Regarding studies of circulating FABP4 levels, we recently demonstrated that FABP4 contributes to blood pressure elevation in hypertensives, and elevation of FABP4 levels is predisposed by a family history of hypertension (*Am J Hypertens* 2012). We also showed the association of FABP4 levels with insulin resistance (*PLoS One* 2013) and cardiac diastolic dysfunction (*Cardiovasc Diabetol* 2014). Furthermore, we firstly revealed that FABP4 level would be a novel predictor of cardiovascular events (*PLoS One* 2011).

The Tanno-Sobetsu Study

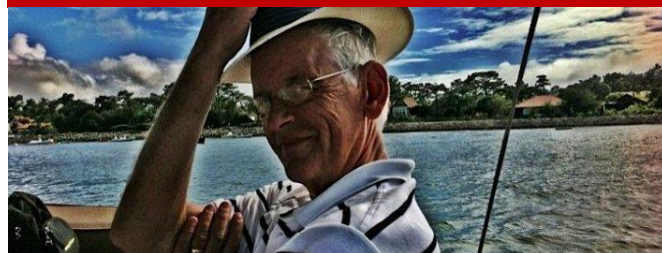


Sobetsu Town in the Tanno-Sobetsu Study

As a collaboration with the Department of Public Health in Sapporo Medical University, we have been conducting the Tanno-Sobetsu Study, a study with a population-based cohort design recruiting residents of two rural towns, Tanno and Sobetsu, in Hokkaido since 1978. The Tanno-Sobetsu Study includes annual health

examination, pathophysiological assessment of metabolic syndrome and cardiovascular disease and follow-up survey. Using samples and data of the study, we have previously reported a number of research studies about hypertension, metabolic syndrome, coronary artery disease, cerebrovascular diseases and diabetes mellitus. Our results are now cited in several guidelines for treatment of diseases, including hypertension, as evidences in Japan.

Lars - a remarkable man



For those of you who read this ISH newsletter and who have participated in ISH activities, you will know Lars Lindholm as the mastermind behind many successful ISH-related initiatives, as Past-President and as the Editor of the fantastic ISH newsletter. What you may not be aware of, is that Lars has had many successes and has contributed to many programmes and causes beyond ISH.

As highlighted in the recent Lancet editorial ([click here](#)), which focuses on the importance of research in general practice, it is impressive to note that Lars was way ahead of his time when he helped build and create Sweden's first National Research School in General Practice, a project that he was involved in soon after he retired (and when reemployed by his old university). This fantastic initiative on the Swedish school is highlighted by Richard Horton in the Lancet Editorial and I encourage you to read it. We are indeed fortunate to have Lars work with us in ISH.

Rhian Touyz
President, ISH



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New ISH Council members

We were delighted to welcome the following new ISH Council members in June.

Masatsugu Horiuchi Tohon, Ehime, Japan



I am carrying out basic and pharmacological research in hypertension as a research-clinician-scientist. My main research interests include the roles of renin-angiotensin system in blood pressure regulation, vascular biology and brain function with particular regard to cognitive function.

Yoshihiro Kokubo Osaka, Japan



I am a chief doctor in the National Cerebral and Cardiovascular Center, Japan. My specialty is preventive medicine and epidemiology, especially related to hypertension and kidney dysfunction. I contribute to many international societies in a variety of capacities and editorial board activities in the areas of hypertension, stroke, and preventive medicine.

Markus Schlaich Perth, Australia



I am the Dobney Chair in Clinical Research at the University of Western Australia, based at the Royal Perth Hospital.

As a clinician-scientist and renal physician I have specific interest in hypertension associated with chronic kidney disease and the role of the sympathetic nervous system in this scenario. My major aim is to

translate evidence from mechanistic studies into clinical practice to improve outcomes for patients with hypertension and associated co-morbidities.

Maciej Tomaszewski Leicester, UK



My research interests focus primarily on genetics and genomics of cardiovascular disorders with a particular emphasis on essential hypertension and its complications. I am also interested in genetic and environmental background of sexual dimorphism in cardiovascular risk (why men develop and die of cardiovascular disorders more frequently than age-matched women).

Richard Wainford Boston, USA



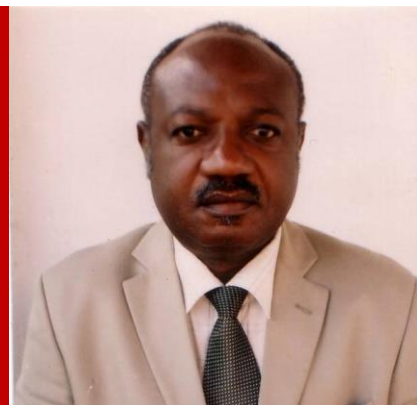
My research interests are focused on understanding the pathophysiology of hypertension, with particular regard to central neural control of the kidney and the implications of this for long-term blood pressure regulation. As such my research is focused on the areas of: Renal Sodium Handling, Neural Control of Blood Pressure, Salt-Sensitive Hypertension.

COUNCIL'S CORNER - HYPERTENSION ISSUES; A PERSONAL VIEW

**Basden
Onwubere**

University of
Nigeria Teaching
Hospital, Enugu
Nigeria

Council member



High Blood Pressure: a high burden in the economically weakened setting!

The prevalence rates of hypertension vary around the world. The overall prevalence of raised blood pressure in adults aged 25 years and over was around 40% in 2008. Even though the proportion of the world's population with high blood pressure, or uncontrolled hypertension, fell modestly between 1980 and 2008, because of population growth and ageing, the number of people with uncontrolled high blood pressure rose from 600 million in 1980 to nearly 1 billion in 2008.

There is, therefore clear evidence that global prevalence of hypertension has been increasing. In 2000, 972 million people had hypertension with a prevalence rate of 26.4%, 333 million in economically developed countries and 639 million in economically developing countries. It is projected that by 2025 a total of 1.54 billion people accounting for 30% of the World population will be hypertensive with 75% of these from developing countries and regions. This means that 3 out of 4 people with high blood pressure will be living in low and middle income countries. It is ironic that this scourge targets economically weakened and unwary populations that are of course ill-prepared to combat it.

Despite the documented evidence of high burden of high blood pressure (HBP) in economically disadvantaged populations, most current efforts to combat the scourge appear skewed towards populations with a lower burden. Because both awareness and control rates remain significantly lower in low and middle income countries (LMIC) than in higher income settings, there is a need for control strategies to be concentrated on those with a higher disease burden.

Surprisingly, only few countries in LMIC have developed Guidelines for management of HBP, some that have developed are not updated regularly. For instance, the Guidelines for management of HBP in sub-Saharan Africa was published in the Journal of

Hypertension in 2003 - the review process has only just started 11 years later. There is a need to encourage Regional and National Hypertension Societies in LMIC to develop Guidelines for the management of HBP in their settings to promote awareness and guide local healthcare personnel.

References

1. Sliwa K, Stewart S, Gersh BJ. Hypertension: A Global Perspective. *Circulation*. 2011;123:2892-2896
2. Global health risks: mortality and burden of disease attributable to selected major risks. Geneva, World Health Organization, 2009 (http://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdf).
3. World Health Statistics 2012. Geneva, World Health Organization, 2012
4. Lemogoum D, Seeday YK, Mabadeje AFB, Onwubere BJC, et al. Recommendations for prevention, diagnosis and management of hypertension and cardiovascular risk factors in sub-Saharan Africa. *Journal of Hypertension* 2003; 21: 1-8
5. Mendis S1, Lindholm LH, Anderson SG, Alwan A, Koju R, Onwubere BJ, et al. Total cardiovascular risk approach to improve efficiency of cardiovascular prevention in resource constrained settings. *J Clin Epidemiol*. 2011 Dec;64(12):1451-62.

**Maciej
Tomaszewski**

University of Leicester
Leicester
UK

Council member



Resistant hypertension and non-adherence to antihypertensive treatment

Approximately 10-20% of hypertensive patients are labelled as resistant to treatment. It has always been argued that a large proportion of these patients are actually pseudo-resistant to antihypertensive therapy and the recorded blood pressure (BP) elevations are frequently due to white coat effect, inappropriate measurements, clinical inertia or therapeutic non-adherence. Unavailability of direct and objective tests to confirm/exclude non-adherence has made this form of pseudo-resistant hypertension diagnostically challenging.

The recent transition of methodology widely used in forensic medicine labs [high performance liquid chromatography mass spectrometry (HPLC-MS/MS)] to blood pressure clinics has provided us with a new tool of screening for non-adherence to antihypertensive therapy using a single spot-urine sample. This highly sensitive and specific assay detects the presence of all commonly prescribed antihypertensives in urine. It has been instrumental in revealing alarmingly high rates of non-adherence to antihypertensive therapy in specialist centres (1,2). Almost one in four hypertensive patients is either partially or completely non-adherent to antihypertensive treatment based on the results of HPLC-MS/MS urine analysis (2). The non-adherent patients have significantly higher values of clinic and 24-hour ambulatory BP and there is a clear correlation between the degree of non-adherence to treatment and the magnitude of BP elevation (1). Therapeutic non-adherence is particularly common amongst patients referred to renal denervation (2). Although the biochemical screening for non-adherence to antihypertensive treatment by HPLC-MS/MS has several limitations, it has become a practise changing application - we can now identify a common form of pseudo-resistant hypertension prior to unnecessary treatment escalations and/or expensive diagnostic tests and procedures. Nonetheless, there is still uncertainty on how to approach non-adherence to antihypertensive treatment in the clinical setting.

Here in Leicester, we use the results of biochemical screening for non-adherence to treatment as an opener to conversation with patients. In the spirit of multi-disciplinary team care we ask our patients' GPs to take part in the process to improve adherence. In many cases of biochemically confirmed non-adherence to treatment, simple measures such as good communication and simplification of drug regime have been successful in improving regular administration of medications and translated into better BP control. It should be acknowledged that it is much harder to tackle intentional non-adherence that stems from certain beliefs around hypertension, its complications and BP lowering treatment. More research is needed to find the most effective strategies to manage non-adherence to antihypertensive treatment.

It is worth pursuing studies in this poorly investigated area - better adherence to antihypertensive treatment means better BP control, better individual and population-wide cardiovascular outcomes and reduction in economic costs to health-care (due to drop in referrals for expensive diagnostic procedures/therapies to manage resistant hypertension).

1. Jung O, Gechter JL, Wunder C, Paulke A, Bartel C, Geiger H, Toennes SW. Resistant hypertension? Assessment of adherence by toxicological urine analysis. *J Hypertens*. 2013;31:766-74.
2. Tomaszewski M, White C, Patel P, Masca N, Damani R, Hepworth J, Samani NJ, Gupta P, Madira W, Stanley A, Williams B. High rates of non-adherence to antihypertensive treatment revealed by high-performance liquid chromatography-tandem mass spectrometry (HP LC-MS/MS) urine analysis. *Heart*. 2014;100:855-61.

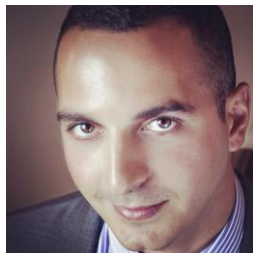
ISH New Investigator Committee Update

Right: New NIC logo



Athens June 2014 ISH New Investigator Meeting Programme

Athens, the capital and largest city of Greece, hosted the 4th ISH New Investigator Meeting Programme in June. This programme once again provided scientists and clinicians (under 40 years of age) in training who have an interest in hypertension and cardiovascular disease with opportunities to present their research and meet their peers.



Fady Hannah-Shmouni
NIC Working Group member

The programme was exclusively organized and executed by the ISH New Investigator Committee (NIC).

The programme's kick-off event was held on 13th June on the rooftop of the Divani Caravel Hotel, overlooking the city. This was an exciting opportunity to hear about some research conducted by brilliant young investigators from across the globe, and for new society mentees and mentors to connect over wine and dinner.

Highlights of the event included the release of the new ISH NIC logo (shown above) and the launch of the ISH Mentorship Scheme.



Left: New Mentor and Mentee

Stephen Harrap and Junhua Zhou

Fadi Charchar (Leader, Networking and Mentorship New Investigator Working Group) stressed on the importance of collaboration between young scientists and the various opportunities that exist through the ISH New Investigator Network.

The ISH New Investigator Meeting Programmes and symposia provide a unique opportunity for young

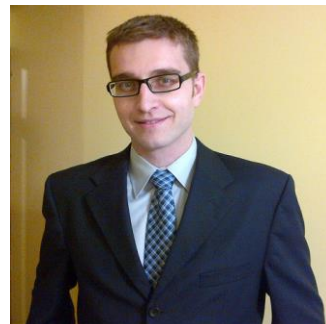
investigators to present and discuss, make new friends, build research networks and establish collaborations that can last a lifetime and a platform for them to excel in their field of scientific work.

The NIC pledges to continue its dedicated work and looks forward to welcoming several new investigators to membership that have been successfully recruited since the Hypertension Athens meeting.

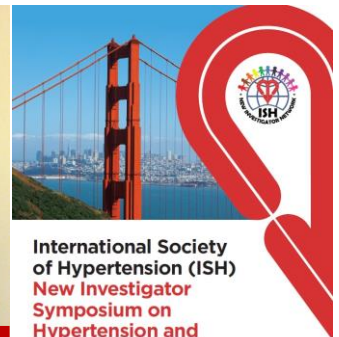
See page 11 for a list of award winners presented as part of this programme.

Contribution from Fadi Hannah-Shmouni
NIC Working Group Member / New Haven, USA

5th ISH New Investigator Symposium on Hypertension & Cardiovascular Disease



Dylan Burger
Communications Committee / NIC Member



International Society of Hypertension (ISH)
New Investigator Symposium on Hypertension and Cardiovascular Disease

Monday 8th September 2014
Hilton San Francisco Union Square

The 5th ISH New Investigator Symposium on Hypertension and Cardiovascular Disease was held on 8th September in collaboration with the American Heart Association Hypertension Council in advance of their 2014 Scientific Sessions. Organized exclusively by members of the ISH New Investigator Network the half day symposium featured 14 oral presentations and over 60 posters from the best young scientists in the field of hypertension.

The sessions featured world-class science and there was excellent scientific discussion by participants. Two oral prizes and five poster prizes were awarded to investigators across a range of clinical and preclinical topics. As always the symposium also provided an opportunity to interact and network with peers. Several senior scientists were also present allowing young investigators the opportunity to discuss their research with field leaders in a non-threatening environment.



The symposium was capped by a keynote lecture from Dr. Gabriel Navar who spoke on the transition from

mentee to mentor for scientists and the importance of mentorship throughout a scientific career. The talk was informative and frank with Dr. Navar frequently providing his own personal experiences as mentor and mentee. We thank Dr. Navar for his participation and for continuing the lofty standard of lectures that has typified each New Investigator Symposium

The symposium would not have been possible without the generous support of our sponsors (as listed below) and the ISH New Investigator Committee graciously acknowledges their support.

Sponsors of the ISH NIC in 2014

American Heart Association Council on Hypertension, AtCor, Boehringer Ingelheim, Daiichi-Sankyo, DSI, Omron Europe

Journals: Clinical Science, Hypertension Research, Journal of Human Hypertension

Award winners (shown and listed below):



- Trevor Hardigan
- Cam McCarthy
- Urmi Basu
- Sarah Even
- Hana Itani
- Ashley Wagoner
- Shyamala Thirunavukkarasu



The symposium was organised by the ISH New Investigator Committee. Committee members are shown above with Dr. G. Navar - keynote speaker.

Dylan Burger
NIC and Communications Committee member
Ottawa, Canada

HYPERTENSION ATHENS

Joint ESH-ISH Meeting

13-16 June 2014

The Hypertension Athens June meeting was a great success and welcomed nearly 5,000 delegates of different medical specialities (including cardiology, internal medicine, general medicine, nephrology, endocrinology and diabetology) from all corners of the world.



The scientific programme covered a range of topics from epidemiology to therapeutics, with more than 2,200 original abstracts being presented (363 as oral communications and 1,909 as attended posters). The leading countries contributing abstracts were: Russia, Greece, Italy, Japan, Spain, China, South Korea, Ukraine, Argentina, and Poland.

The Society would like to extend its sincere appreciation to Professor Manolis and the Organizing Committee for their tremendous efforts and for such a successful outcome of this Joint ESH-ISH Meeting.

- **ISH 2014 Award and Prize Winners**
- **ISH 2014 Franz Volhard Lecture by Toshiro Fujita**
- **ISH/WHL Dietary Salt Session**
- **ISH/ESH 2020 Glasgow Scientific Meeting**
- **Hypertension Athens Santorini Satellite Meeting: "Putting the A back into RAAS"**

A report on the ISH Athens New Investigator Meeting Programme can be viewed on page 8.

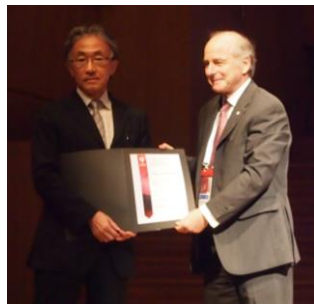


2014 Award and Prize winners

We would like to congratulate the following ISH Award and Prize winners at the June Athens Meeting.

Franz Volhard Award and Lectureship for Outstanding Research

This award and lectureship was endowed by Farbwerke Hoechst in 1972 to commemorate the centenary of the birth of Franz Volhard. The award shall be made at *ISH Scientific Meetings* to a person or persons who, in the opinion of the ISH Awards Committee of the ISH, shall have initiated in the field of hypertension or in a related discipline, a concept which remains of current interest.



Recipient: **Toshiro Fujita**

University of Tokyo,
School of Medicine
Tokyo, Japan

A report follows on P. 12-13 from Toshiro Fujita regarding his award lecture given at the meeting.

ISH Robert Tigerstedt Lifetime Achievement Award

The award is presented to a person, persons or institution responsible for distinguished work relating to the aetiology, epidemiology, pathology or treatment of high blood pressure. The achievements of the recipient should reflect distinguished contributions in research, teaching or clinical activities relating to the aetiology, epidemiology, pathology or treatment of high blood pressure and successful mentorship of younger colleagues.



Recipient: **John Funder**
University of Melbourne
Australia

AstraZeneca Award

The award was endowed by Astra Pharmaceuticals AB in 1979. It is presented on the recommendation of the Awards Committee of the ISH to a distinguished investigator responsible for outstanding work related to clinical pharmacology and therapy of arterial hypertension.

AstraZeneca has provided a sponsorship grant towards this independent Programme.



Recipient: **George Bakris** University
of Chicago USA

ISH Paul Korner Award supported by the High Blood Pressure Research Foundation

This award was endowed by the High Blood Pressure Research Foundation in 2013 to honour the late Paul Kroner, an internationally renowned expert in the field of hypertension with a special interest in the neuroscience of blood pressure. The award is presented to a person who has demonstrated outstanding contributions to research on hypertension in the broad field of neuroscience.



Recipient: **Geoff Head**
Baker IDI Heart & Diabetes
Institute
Melbourne, Australia

ISH Developing World Award



This award is for a researcher in the developing world who has done outstanding work in the region.

Recipient: **Yakoob Seedat**
Nelson R Mandela School of Medicine
University of Kwa Zulu Natal
Durban, South Africa

ISH New Investigator Oral Presentation Awards, supported by Daiichi-Sankyo

These awards were established in 2012 to encourage New Investigators and recognise excellence in scientific contribution at the ISH Biennial Scientific Meetings and will be awarded to New Investigators judged from a group of finalists to have given the best oral presentations.



Winner:

Lucinda Hilliard
(Australia)



Runner Up:

Muhammad Oneeb Rehman Mian
(Canada)

ISH New Investigator Poster Presentation Awards, supported by Daiichi-Sankyo, Clinical Science, Hypertension Research and the Journal of Human Hypertension

BASIC SCIENCE AWARD:

Winner: Silvia Monticone (Italy)
 Runner Up: Katrina Mirabito (Australia) - shown right



CLINICAL SCIENCE AWARD:

Winner: Aurélien Lorthioir (France) - shown right



Runner Up: Maria Gosk (Poland)

POPULATION SCIENCE AWARD

Winner: Nicolas Verheyen (Austria) - shown right



Runner Up: Yi Zhang and co-author Chenhui Tai (China)

Austin Doyle Award supported by Servier Australia

This award was endowed by Servier Australia to mark the contribution of Austin Doyle, Past-President of the ISH and Founding Chairman of the High Blood Pressure Research Council of Australia. It is awarded to a graduate, who is within 5 years of post-graduate qualification.



Recipient: **Vikas Kapil**
 Queen Mary University of London
 London, UK

Distinguished Membership Award



Members who have given outstanding service to the ISH and have made unusually distinguished contributions to experimental and clinical research in hypertension may be nominated to be distinguished Members of the Society.

Recipient: **John E Hall,**
 University of Mississippi Medical Center, USA

ISH International Forum Poster Prizes

ISH International Forum Poster Prizes will be in Basic science (supported by ISH and Clinical Science), Clinical science (supported by Daiichi-Sankyo) and Population science.

African Region:

- Basic science: Ruan Kruger (South Africa)

Asia & Australasia Region:

- Basic science: Jagriti Bhatia (India)
- Population science: Hiroyuki Takase (Japan)
- Clinical science: Jin-Ok Jeong (South Korea)

Central and South American Region:

Basic science: Carolina Caniffi (Argentina) *

* Dr. Costa, first author, sadly passed away before the ISH could award her this prize. We would like to send our sincere condolences to her family and friends.

- Population science: José Boggia (Uruguay)
- Clinical science: Brunella Mendonça Chinem and colleagues: Ana Luiza Lima Sousa, P.B. Jardim, A. Arantes, R.R. Bernades, A. Souza, M. A. Barbosa, L.F. Portilho. T. S. Jardim, G.C. Guimarães- Filho (Brazil)

Eastern Europe & Middle East Region:

- Basic science: A. Sydorhuk (Ukraine)
- Clinical Science: Elena Ardeleanu (Romania)



(shown below)

- Population science: Valeria Regecová (Slovak Republic)

Western Europe and North American Region:

- Basic science: Mohammad Newaz (USA)
- Clinical science: Christos Chatzikyrkou (Germany)
- Population science: Stamatis Efstathiou and colleagues: Irini Skeva, E. Zorbala, E. Georgiou, T. Mountokalakis I. Skeva (Greece)

The International Forum of the ISH embodies and nurtures the global nature of the Society and was first established in 1992.



ISH
 AFFILIATED SOCIETY

Today the International Forum is chaired by ex-ISH President Ernesto Schiffrin (Canada) with Jeong Bae Park (Korea) and Yoshihiro Kokubo (Japan) as Forum Officers. It is a consultative forum, the mandate of which is to establish effective liaison between the ISH and National Societies of Hypertension or Councils of High Blood Pressure Research. It also provides a unique infrastructure and platform for networking and "cross-talk" between Societies.

View a recording of the Hypertension Athens Opening Ceremony. [Click here](#)

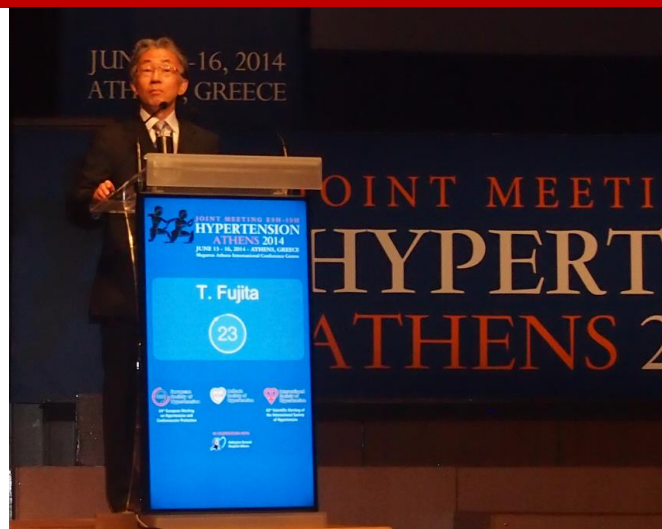
ISH 2014 Franz Volhard Lecture

June, Athens, Greece

Two Novel Pathways in Salt-Sensitive Hypertension

Toshiro Fujita

Department of Clinical Epigenetics, Research Center for Advanced Science and Technology (RCAST), The University of Tokyo, Tokyo, Japan



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The most obvious connection between sodium intake and health is manifested by the relationship between sodium intake and blood pressure (BP). Different individuals have different susceptibilities to the BP-raising effects of salt. The BP sensitivity to salt is defined as the inter-individual difference in the BP response to changes in dietary sodium chloride intake. Studies by Guyton revealed an interaction between genetically determined alterations in the kidney and excess dietary sodium intake. Renal excretory function is impaired in patients with salt-sensitive hypertension, and result in an elevated BP. Both the aldosterone/mineralocorticoid receptor (MR) and the renal sympathetic nervous systems (SNS) play important roles in the regulation of renal excretory function and blood pressure control. However, the mechanisms underlying these processes remain to be elucidated. Recent studies reveal the activation of two pathways involving MR and glucocorticoid receptor (GR) in salt-sensitive hypertension.

Rac1, a member of the Rho family of small GTP-binding proteins, serves as a novel ligand-independent modulator of MR activity (Shibata S et al. *Nat Med* 14:1370-1376, 2008). In Dahl salt-sensitive (S) rats, salt loading activates renal Rac1, which in turn leads to MR activation, sodium retention, and BP elevation, despite reduced levels of plasma aldosterone, whereas in Dahl resistant (R) rats and normotensive rats, Rac1 activity is normally reduced by salt loading and is associated with a decrease in MR activity, a normal sodium state, and normal BP. It suggests paradoxical response to MR activity to salt loading in Dahl S rats. Given the finding that treatment with the Rac1

inhibitor reduces BP by reversing the increase in renal Rac1 and MR activity, the paradoxical response of MRs to salt loading in salt-sensitive hypertension is attributable to the abnormal response of Rac1 to salt (Shibata S et al. *J Clin Invest* 121: 3223-5243, 2011).

In salt-sensitive hypertensive rats, therefore, salt loading causes the aberrant Rac1-MR pathway to increase sodium reabsorption in the aldosterone-sensitive distal nephron, and leads to salt-sensitive hypertension.

Another important factor influencing the salt-sensitivity of BP is the renal SNS. Salt loading increases renal SNS activity in salt-sensitive hypertensive rats, but it remains unclear how increased SNS activity in the kidney enhances tubular sodium reabsorption and leads to the development of salt-sensitive hypertension. We found that salt loading increases renal sympathetic activity, which plays a key role in the development of salt-sensitive hypertension through the aberrant α -adrenergic stimulant-GR-WNK4-sodium chloride co-transport (NCC) pathway in the distal convoluted tubules (Mu SY, et al. *Nat Med* 17:573-580, 2011). The continuous infusion of norepinephrine in mice activates the WNK4-NCC pathway, leading to sodium retention and the resulting salt-induced BP elevation. Treatment with the α -blocker propranolol reversed these norepinephrine-induced changes. Thus, the α -adrenergic receptor (AR) plays a critical role in the norepinephrine-induced activation of the WNK4-NCC pathway. Given the finding that both renal WNK4 down-regulation and salt-sensitive hypertension during the isoproterenol infusion were absent in distal nephron-specific GR-KO mice, GRs are indispensable for the α -AR stimulation-induced activation of the WNK4-NCC pathway in DCT cells and the resulting salt-sensitive hypertension.

NCC activation is involved in salt-sensitive hypertension in rodent models via two novel pathways: the Rac1-MR-NCC and α AR-GR-WNK4-NCC pathways. An aberrant Rac1-MR pathway increases

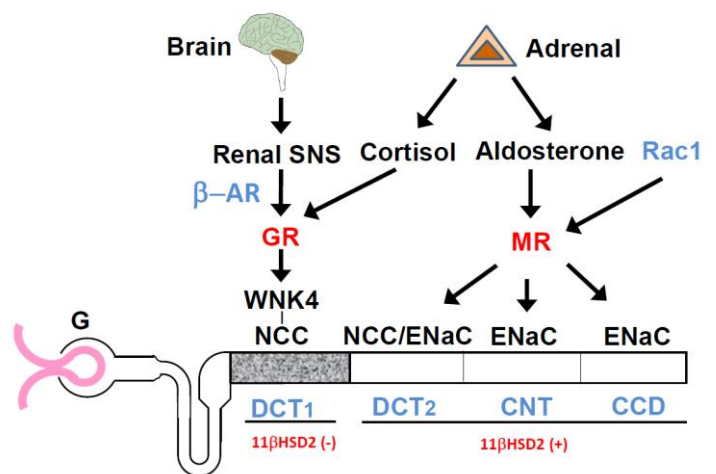
sodium reabsorption by activating NCC in the DCT2 segment, in addition to activating epithelial sodium channels (ENaC) in the DCT2, connecting tubule (CNT) and collecting duct (CD) segments, whereas an aberrant α AR-GR-WNK4 pathway activates NCCs in the DCT1 segment. Mineralocorticoid specificity is achieved by the 11 β -hydroxysteroid dehydrogenase type 2 (11 β -HSD2), which converts cortisol to cortisone, an inactive metabolite. The aldosterone-sensitive distal nephron is characterized by high expression levels of 11 β -HSD2; however, 11 β -HSD2 is absent from the DCT1 segment. As a result, aldosterone serves as a ligand for MR in the DCT2, CNT and CD segments, whereas cortisol, rather than aldosterone, serves as a ligand for MR in the DCT1 segment (**Figure**). With the presence of abundant cortisol in the DCT1 cells, the activated GR leads to α -AR competence to allow activation of the WNK4-NCC pathway in response to stress. On the other hand, MR activation in the DCT2 segment also causes NCC activation via Sgk1. The nuclear receptors, MR and GR, play a role in impaired renal excretory function and the resulting salt-sensitive hypertension, by increasing sodium reabsorption at different tubular segments (Fujita T. *J Am Soc Nephrol* 25:1148-55, 2014).

Salt-sensitive hypertension can be produced in animals by genetically engineering key neurohormonal regulators. We found that two novel pathways involving the adrenal and sympathetic nervous systems (Rac1-MR-Sgk1-NCC and the renal SNS-GR-WNK4-NCC pathways) play crucial roles in certain rodent models of salt-sensitive hypertension. These pathways stimulate the nuclear receptors, MR and GR, to activate NCC in the different DCT segments, resulting in abnormal renal excretory function and increased BP. Furthermore, it is possible that the aforementioned mechanism identified in rodent models may be related to those found in salt-sensitive humans. The two pathways provide alternative therapeutic targets for salt-sensitive hypertension and salt-mediated cardio-renal injury. However, further studies are required to assess the therapeutic value of

manipulating these particular pathways.

Figure (below).

Two novel pathways (Rac1-MR-NCC/ENaC and α AR-GR-WNK4-NCC pathways) involving adrenal and central/sympathetic nervous systems (SNS) in salt-sensitive hypertension. 11 β -HSD2 is absent in the DCT1 segment but present in the other tubular segments. MR; Mineralocorticoid receptor, GR; glucocorticoid receptor, 11 β -HSD1; 11 β -hydroxysteroid dehydrogenase type 1, α -AR; α -adrenergic receptor, DCT; distal convoluted tubule, CNT; connecting tubule, CD; collecting duct; NCC; sodium chloride co-transporter, ENaC; epithelial sodium channel, G; glomerulus.



Odd Corner:

Article from
The Lancet
July 1907

CATS AS A PREVENTIVE OF PLAGUE.

Under the head of "Notes and News" in the *Journal of Tropical Medicine and Hygiene* dated July 1st it is stated that "Lieutenant-Colonel Buchanan took a cat census of certain villages that enjoyed exceptional immunity from plague and of others that had been severely handled by the disease." The result showed that the immune communities harboured large numbers of cats, whereas in those that suffered the animals were scarce. Our contemporary is of opinion that "the expedient is one that is certainly worthy of attention, though it is difficult to see how the keeping of cats can be spread more widely by official action."

[JULY 27, 1907.]

THE LANCET,]

ISH/WHL Dietary Salt Session Hypertension Athens Meeting

Dan Lackland

World Hypertension
League
Vice President /
President Elect



A focused session on the current issues regarding dietary salt with effects on blood pressure levels and hypertension-related high blood pressure and hypertension was held during the 2014 joint conference of the European Society of Hypertension (ESH) and the International Society of Hypertension (ISH) in Athens Greece. The program was co-sponsored by ISH and the World Hypertension League and chaired by Professors Ernesto L. Schiffrin (McGill University, Montreal Canada) and Daniel T. Lackland (Medical University of South Carolina, Charleston USA) - shown below.



Session faculty are shown left

The current global perspectives of salt intake and cardiovascular risk were presented by the session faculty including Dr Norm Campbell (Libin Cardiovascular Institute of Alberta, Calgary), Dr Graham MacGregor (Wolfson Institute of Preventive Medicine, London, UK), and Dr Elizabeth Dunford (George Institute for Global Health, Australia). While there is no “debate” over the dangers of dietary salt as a cause of cardiovascular disease and stroke, there is a clear need for:

- health care professionals to take a more active role educating the public and patients of the risks of salt intake,

- high-quality science to provide evidence for design of interventions,
- Implementation of initiatives to reduce salt intake at the population level.

The issues of debate include the specific details of salt intake levels for specific populations. A key point of the session addressed the issue identifying the “controversy” of dietary salt with heart disease and stroke as a result of weak research methodology and/or commercial influence. The session reported that most of the effort to reduce dietary salt is not based on data from multiple randomized trials with hard outcomes but observational and epidemiological data. Further, with the large amount of salt intake throughout the world, there are few studies in populations consuming less than 2300 mg of sodium per day.

In addition, recommendations of salt intake are confused with low-quality studies that include flawed and invalid measures of sodium consumption. Superficially, the use of spot urine analyses represents an inaccurate and inappropriate means of estimating sodium consumption. This methodology with single non-standardized blood pressure measurements can result in significant bias and imprecise risk estimates in population studies. The spot urine analysis was a limitation of the Prospective Urban Rural Epidemiology (PURE) study being cited as showing that most of the world eats much higher levels of sodium than those recommended by most international organizations. However, this is an example of a study that had failed to measure salt in an appropriate and valid manner with an inadequate formula to estimate salt intake.

Further, the extent of commercial interference on study design, implementation, and interpretation must be considered with salt intake and outcomes research. There are concerns that some academics have significant financial interests in the salt and food industries who have published in very prominent journals. However, when international and national organizations have done rigorous reviews of the literature, omitting low-quality data, conclusions clearly support lowering salt intake to prevent stroke and cardiac disease. The WHL has recently put out a call for the setting of research standards related to dietary salt, to try to promote the inclusion of valid measurements in high-quality science with reliable results. In addition, the WHL is putting together a global coalition of national and international organizations to oversee those standards.

The global impact of reduced salt intake is quite significant with a 2-g drop in the amount of salt consumed per day translating to a 20% reduction in cardiovascular events. Based on a 2010 Institute of Medicine (IOM) report, approximately 32% of hypertension cases are caused by high dietary salt—a number that translates into about 300 million people worldwide. Further The Global Burden of Disease Study estimates over three million deaths, 61 million years of disability, and 57 million years of life lost were related to high dietary salt in 2010.

There have been significant global strides in implementing reductions in dietary salt, primarily tackling processed foods and launching public-education initiatives with 60 initiatives implemented during the past four years alone. These efforts have been successful with significant effects. For example, Finland, which has one of the longest-running public salt-reduction initiatives, lowered salt intake by 15% between 1979 and 2007, from 12.8 g to 9.0 g. Likewise, The UK reduced intake by 15% between 2001 and 2011, from 9.5 g to 8.1 g, saving an estimated 8500 lives per year. The Session clearly identified the reduction of salt intake as a major global initiative for the reduction of cardiovascular disease and stroke, and an effort with great potential impact on world health.

Inaugural Renin-Angiotensin Aldosterone System Meeting:

“Putting the A back into RAAS”

Santorini, Greece, 10-12 June 2014
Official Satellite to 2014 ESH/ISH Meeting,
Athens, Greece

Anastasia Susie Mihailidou and
Louise Burrell

This meeting report for our Investigator-Initiated Satellite is provided on behalf of our Organising Committee members: Anthony Ashton, George Bakris, Robert Carey, Mark Cooper, Kate Denton, Carlos Ferrario, Toshiro Fujita, Peter Fuller, John Funder, Stephen Harrap, Frederic Jaisser, Colin Johnston, Martin Reincke, Michael Stowasser, Rob Widdop, Morag Young and our Secretariat, Jennifer Seabrook.



As indicated by the name, the renin-angiotensin-aldosterone system (RAAS) has three important components, renin, angiotensin and aldosterone. The RAAS is an integrated system that not only regulates blood pressure, electrolyte and fluid balance, the classical actions of RAAS, but is also involved in cardiovascular disease, metabolic syndrome and many other conditions. Our focused meeting provided the

ideal interactive forum for the latest research developments by leaders in this field as well as opportunity for young investigators and students to present their research. Clinical



and basic research into the regulation of RAAS in the brain, vessels, kidneys, heart and primary aldosteronism were presented. Novel techniques for both advancing research and clinical diagnosis stimulated discussion and facilitated new collaborations. Our report highlights some of these developments which were presented by our invited speakers.

It was truly an international meeting with over 50 delegates travelling from 14 countries - Australia, Austria, Canada, China, Denmark, France, Germany, Greece, Ireland, Italy, Japan, Sweden, United Kingdom and United States - to present their research, exchange ideas and establish new friendships. Securing funding was challenging and we thank our sponsors, European Society of Endocrinology, Daiichi Sankyo, Attoquant Diagnostics, Dia Sorin, Mitsubishi-Tanabe, Servier, seed funding from Dr John Funder and the COST Network for their support, which enabled this meeting to be held.

As an Official Satellite of ESH/ISH Hypertension 2014, the first presentation was appropriately “Hypertension Management in the 21st Century: Is there a role for renal denervation?” by Dr George Bakris who provided an overview of hypertension management. Although there are 9 distinct classes of antihypertensive medications, five of which influence the RAAS, control of hypertension continues to be a challenge, with NHANES 2010 reporting that only 53% of patients with hypertension achieve goal BP <140/90 mmHg. Lack of control can be due to patient non-adherence due to either side effects/tolerability of medications or refusal to accept treatment for hypertension, a silent disease. Therefore other options have been investigated such as baroreceptor activation therapy (BAT) and renal denervation. Although early studies suggested that renal denervation would provide benefit to reduce BP, the results of the SYMPPLICITY HTN-3 trial failed to confirm this. Trials of BAT in hypertension and heart failure are ongoing, and early results appear promising.

The increasing aging population globally will place an enormous burden on health services. Understanding the changes in the body’s homeostatic mechanisms with advancing age is paramount for targeted treatment. Exciting data from the laboratories of Dr Kate Denton and Dr Iris Jaffe identify important changes in RAAS with aging. Males have low renal angiotensin type 2 receptor (AT2R) expression throughout life, whereas in females AT2R expression is high during puberty and then declines with advancing age. Impaired vascular function with advancing age may indicate changes in smooth muscle cell (SMC) mineralocorticoid receptors (MR) or “aldosterone receptors.” Mice in which MR was selectively deleted from SMC had decreased blood pressure with advancing age and reduced vascular myogenic tone and agonist-dependent contraction.

RAAS also has an important role in mediating innate and adaptive immune responses during cardiovascular disease, which Dr Ernesto Schiffrin highlighted in his presentation. Experimental studies mirror the changes observed in humans, suggesting new therapeutic approaches to improve outcomes in hypertension and cardiovascular disease. MR also have an important role in the hypothalamic paraventricular nucleus (PVN) shown in studies conducted by Dr Elise Gomez-Sanchez where activation of MR within pre-autonomic neurons in the PVN directly participate in regulation of sympathetic nervous system drive.

It is certainly an exciting period in RAS research with selective non-peptide AT₂ receptor (AT₂R) agonists now identified. Dr Robert Widdop provided results from their studies with CGP42112, Compound 21 or angiotensin peptides that showed cardiovascular protection in various models such as cardiac fibrosis and atherosclerosis. This was followed by Dr Robert Carey presenting his studies showing activation of intra-renal AT₂R with intravenous Compound 21 increased urinary Na⁺ excretion and renal proximal tubule cell apical membrane AT₂R protein, while lowering BP in Ang II-dependent hypertension and a potential therapeutic target for the treatment of fluid retaining states and hypertension. Interesting computer modelling studies of AT₂R and the potential for developing novel ligands were presented by Dr Andreas Tzakos. The importance of identifying common pathways in pathologies other than cardiovascular disease was highlighted by Dr Ulrike Muscha Steckelings. Anti-inflammatory and immunomodulatory actions of the AT₂R attenuate inflammation and cartilage destruction in rheumatoid arthritis and can reduce neurological symptoms in experimental autoimmune encephalomyelitis. In both studies, treatment of mice with an AT₂R agonist modified T-cell response reducing TH1-TH17 T cells and increasing regulatory T-cells. Another potential application for AT₂R stimulation is in the field of dermatology with beneficial effects of AT₂ agonists in psoriasis. Various agonists for AT₂R and the MAS receptor are now in preclinical and clinical development for a variety of diseases, both cardiovascular and non-cardiovascular.

Convergent pathways between Ang II and aldosterone were highlighted by Dr David Pearce and Dr Toshiro Fujita. Dr Pearce's laboratory has shown SGK1 is an important regulator of ion transport in multiple segments throughout the kidney and at the transcriptional level, regulated by aldosterone. Their recent data shows that its activity is also regulated by Ang II through an mTOR dependent phosphorylation. Interestingly, Ang II-induced phosphorylation is specific to SGK1; the serine-threonine kinase, Akt, a close relative of SGK1 is not phosphorylated in response to Ang II. Dr Fujita has identified Rac1, a member of the Rho-family of small GTP binding proteins, as a novel ligand-independent modulator of MR activity. Renal Rac1 is activated by salt loading in Dahl salt-sensitive rats and All-overexpressed mice, leading to MR activation despite suppressed serum levels of aldosterone, leading to elevated BP and renal injury. The renal actions of RAAS continued with presentations by Dr Marc Lombes. MR are highly expressed in the distal nephron where there are large variations in extracellular fluid tonicity, establishing an osmotic

gradient which regulates ion and water transport, modulated during renal development and possibly various kidney diseases. Novel findings by Dr Lombes' laboratory show that hypotonicity increases renal MR abundance and further studies are in progress to determine whether this may indicate a pathophysiological role in kidney disease, hypertension or mineralocorticoid resistance.

Similar to the exciting new research developments in selective non-peptide AT₂R agonists and angiotensin peptides and their application, there is increasing interest in understanding MR structure and the determinants for tissue and ligand-specific activation. Dr Peter Fuller and his team have identified proteins which interact in the presence of ligand, either aldosterone or cortisol but not both and confirmed coactivators for the full-length human MR. Ongoing studies are planned to identify ligand-specific interactions as well as antagonism for MR which may lead to developing tissue specific agents. Dr Frederic Jaïsser highlighted the new developments in activation of aldosterone and MR signaling pathways in



endothelial and vascular smooth muscle function.

Primary aldosteronism (PA) is recognized as the most common cause of secondary hypertension for 2-10% of patients with hypertension. The latest developments were presented by many of the leaders in this field in a dedicated session. Dr Maria-Christina Zennaro has established a genome-wide strategy to explore the genetics and genomics of aldosterone-related disorders and provided the introduction to this stimulating session. Dr Martin Reincke followed with presentation of his interesting research into examining the specificity and sensitivity of recently proposed prediction tests for unilateral PA in the clinic and compared the clinical prediction score which includes imaging, serum potassium and glomerular filtration rate to the combination of visible unilateral adenoma on imaging and age <40 years. The results confirmed that adrenal venous sampling continues to be a requirement in the majority of patients.

Detection of PA requires measurement of the aldosterone-renin-ratio (ARR) despite limitations in selectivity, sensitivity and interference from several antihypertensive agents. Novel methods for increasing the accuracy and improving diagnosis of PA screening

were presented by Dr Marko Poglitsch. This approach is in the validation phase and provides great promise. Confirmatory tests are also required to document aldosterone production independent of regulation via angiotensin II and include sodium loading manoeuvres such as fludrocortisone suppression testing (FST) and saline suppression testing (SST). Dr Michael Stowasser and his team have observed that recumbent SST lacks sensitivity compared to seated SST and initiated a pilot study to compare the traditional RSST protocol to SSST. The results from this study show that seated SST had better sensitivity than recumbent SST in confirming PA, was well tolerated by the patients, simple and quick to perform without hospital admission required and comparable reliability. Once the aldosterone-producing adenomas are excised, there has been interest by several research teams in developing antibodies to the enzymes involved in aldosterone biosynthesis, CYP11B1 and CYP11B2. Dr Celso Gomez-Sanchez has developed a specific mouse monoclonal antibody against CYP11B2 and a specific rat monoclonal antibody against the CYP11B1 enzyme and presented initial validation studies which show variable staining pattern in aldosterone producing adenomas and multiple different pathological patterns.

A common theme throughout the satellite was that RAAS is an integrated system. Adipocytes express all components, with overexpression of angiotensinogen (ATG) leading to increased fat mass, adipose inflammation, glucose intolerance and insulin resistance, whereas ATG knockout mice had reduced fat mass. Dr Massimiliano Caprio and his team have shown functional MR in adipose tissue, which mediate regulation of adipogenesis and adipose expansion. Addition of MR antagonists improved glucose tolerance in diet-induced obese mice, and counteracted the effects of high-fat diet on white adipose mass. Translating this to patient management, Dr Gail Adler and her team have shown that dysregulated aldosterone physiology predicts the metabolic syndrome in normotensive and hypertensive adults, without other cardiovascular risk factors. Patients with type 2 diabetes mellitus receiving MR blockade had improved coronary flow reserve, which is a measure of coronary microcirculatory function. Activation of RAAS contributes to the pathogenesis of myocardial infarction (MI) and progression to heart failure. Large randomized clinical trials have shown the benefits of targeting blockade of MR, although the exact mechanisms have not been defined. Dr Anthony Ashton presented recent findings from collaborative research with the laboratory of Dr Anastasia Susie Mihailidou demonstrating integrated activation of non-genomic and genomic MR pathways during experimental MI to promote myocardial damage.

It is an exciting time for RAAS research and we look forward to the next integrated RAAS meeting, possibly as a satellite to the 26th Scientific Meeting of the ISH to be held in Seoul, South Korea in September 2016.

**Anastasia Susie Mihailidou
and Louise Burrell**



Glasgow secures prestigious ESH/ISH Joint Scientific Congress in 2020

The European Society of Hypertension and the International Society of Hypertension (ESH/ISH) Joint Scientific Congress 2020, which will take place at the Scottish Exhibition + Conference Centre (SECC) in Glasgow, Scotland.



The bid was delivered in partnership with the University of Glasgow, the British Hypertension Society, Glasgow City Marketing Bureau (GCMB) and the SECC.

Glasgow is widely recognised as a Centre for Excellence in hypertension research, making it the perfect host city for the ESH/ISH Joint Scientific Congress 2020; with a long, distinguished record in cardiovascular research, blood pressure and hypertension. This is evidenced by the unique situation where the President of the European Society of Hypertension, Prof Anna Dominiczak and the President of the International Society of Hypertension, Prof Rhian Touyz are both from the University of Glasgow.

Glasgow has a long history of healthcare innovation, pioneering revolutionary medical technologies to world-wide audiences and the city looks forward to a bright future of ground-breaking life science research tackling public health issues head-on.

Glasgow is one of Europe's most vibrant, dynamic and friendly cities. Easy to get to and easy to get around, the city is the location of the award-winning Scottish Exhibition and Conference Centre (the venue for 2020). Glasgow has a proud history of academic excellence with its universities internationally renowned as centres of learning and research with the second largest student population in the UK.

Delegates can also enjoy Glasgow's many parks, museums and art galleries, many of which are free of charge. Its unique and warm hearted character make it a hit with visitors, and the city's excellent track record in hosting major conferences mean that you can look forward to a congress to remember.

Scotland's cultural capital looks forward to welcoming the ISH and ESH delegates in 2020!

Congratulations to Norm Campbell!



Our heartfelt congratulations go to Norm Campbell. He was appointed to the Order of Canada by His Excellency the Right Honourable David Johnston, Governor General of Canada on 30th June 30 2014.

The Order of Canada, one of Canada's highest civilian honours, was established in 1967, during Canada's centennial year, to recognize outstanding achievement, dedication to the community and service to the nation.



The World Hypertension League 2014 update

The World Hypertension League (WHL), a coalition of national hypertension organizations, is the public health counterpart to the International Society of Hypertension (ISH). The mission of the WHL is to lead and enhance efforts to prevent and control hypertension globally.

The importance of the WHL mission is emphasized by the recent United Nations (UN) Global Health Summit on non-communicable diseases (NCDs) which agreed to nine health targets to be achieved by 2025. The UN health targets included a 25% reduction in hypertension prevalence and a 30% reduction in dietary salt. Further, the Global Burden of Disease Study estimated that 18% of premature deaths and 7% of global disability are related to increased blood pressure placing particular importance on the work of the WHL. Critical to the mandate of the WHL is strong collaboration and working relations with the ISH and the World Health Organization (WHO).

The WHL executive has recently published a strategic approach to hypertension prevention and control that it encourages national organizations to follow (1). It has also recently conducted a needs assessment of national member organizations to identify opportunities to target. The WHL will be prioritizing: 1) reductions in dietary salt, 2) improving the awareness rate of hypertension, and 3) promoting the

integration of hypertension management into chronic non communicable disease programs, specifically the WHO Package of Essential Noncommunicable (PEN) Disease Interventions for Primary Health Care in Low-Resource Settings program (2).

The WHL (with the ISH and other organizations) has developed a policy statement on dietary salt (3), and an action-oriented fact sheet related to dietary salt (4). To address an emerging issue that low quality research is creating controversy and undermining efforts to reduce dietary salt (5), the WHL has responded by leading a call for quality research and the setting of research standards (6). An international coalition is currently being formed by the WHL to develop standards for the conduct of clinical and population research on dietary salt, regular systematic reviews of evidence and, if required, updating dietary salt recommendations. The WHL will further aid national organizations to promote the WHL policy on dietary salt and will be developing standardized power point slides to aid knowledge translation efforts. An expert group under the WHL has also developed suggested terminology to describe dietary salt intake and reductions in dietary salt to promote the use of common terminology (manuscript under review). Individuals and organizations active in efforts to reduce dietary salt can be nominated for certificates of notable achievement or awards of excellence with the inaugural recognition being granted in 2014.

The WHL has also been active in assisting standardization and promotion of screening programs for blood pressure. A WHL work group has just developed a resource to aid blood pressure screening programs develop (soon to be on www.whleague.org). The workgroup was successful in obtaining a grant to field test the resource in Brazil, Cameroon, and Canada. The resource will be revised in 2015 based on field test results and feedback from end users. A separate WHL workgroup has developed standards for analyzing blood pressure surveys (manuscript under review). The latter effort is intended to aid the tracking of efforts to prevent and control hypertension over time and in different jurisdictions as often surveys are analyzed using non comparable methods. With the ISH, the WHL has developed an action-oriented fact sheet for hypertension and will be aiding national organizations develop similar fact sheets specific to their population (7). Individuals and organizations active in efforts to prevent and control hypertension can also be nominated for certificates of notable achievement or certificates of excellence with the inaugural recognition being granted in 2014. A policy statement to support integration of hypertension management into chronic disease management programs and a work group to aid national hypertension organizations assist in that integration is in an early planning phase.

Extensive efforts have been made to increase communications from the WHL. A regular newsletter is being promoted with plans to increase its circulation and the WHL has a new website (www.whleague.org). A long range congress planning committee has been developed to facilitate prevention and control of hypertension with member organizations and individuals. Perhaps most importantly, the WHL now

has an official journal, namely “The Journal of Clinical Hypertension” that provides global access to high quality peer reviewed literature (8). The WHL encourages all people interested in hypertension to sign up for free access ([http://onlinelibrary.wiley.com/journal/10.1111/\(ISSN\)1751-7176](http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1751-7176)).

The WHL currently faces financial challenges but believes its future is bright and that through collaborative action the burden of blood pressure disease can be markedly reduced. ISH members are encouraged to support the WHL, especially if asked to join and support its work groups.

For more information on any of these exciting efforts, please e-mail: CEO@whleague.org

Norm Campbell MD President, World Hypertension League

Mark Niebylski PhD Chief Executive Officer, World Hypertension League

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MEMBERSHIP INFORMATION

ISH Secretariat Contact Details

The ISH Secretariat moved from Hampton Medical Conferences to The Conference Collective on 1st April. Please see below new contact details.

ISH Secretariat



The Conference Collective
Delivering Excellence in Event Management

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Membership subscriptions 2014

Please note (as stated in the Constitution): Membership shall automatically cease upon failure to pay the annual subscription fee for two consecutive years.

If you haven't yet paid your membership fee this year and are interested in retaining your links to the Society, we would be delighted to receive your payment.

Please contact the Secretariat to receive a payment form.

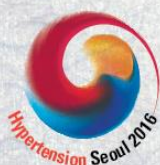
Please help us to recruit new members

If you have a colleague who would like to become a member of ISH please offer to support their application and ask them to complete the online application form that can be found in the Membership section of the Society's website: www.ish-world.com.

Nominations are initially considered by the Membership Committee and ultimately approved by the Society at its Biennial Scientific Meetings.

Please contact secretariat@ish-world.com with any questions

Join us in Seoul in 2016!



Hypertension Seoul 2016

The 26th Scientific Meeting of the International Society of Hypertension

in collaboration with the 11th Congress of the Asian Pacific Society of Hypertension (APSH)
the 25th Annual Scientific Meeting of the Korean Society of Hypertension (KSH)

September 24(Sat) - 29(Thu), 2016
COEX, Seoul, Korea

IMPORTANT DATES:

Opening of Abstract Submissions:	Sept. 24, 2015
Abstract Submission Deadline:	Feb. 24, 2016
Notification of Acceptance:	Apr. 25, 2016
Online Registration Opens:	Sept. 24, 2015
Early Bird Registration Deadline:	May 16, 2016
Pre-Registration Deadline:	Jul. 31, 2016

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