International Society of Hypertension
HYPERTENSION NEWS
December 2014, Opus 39

Notes from the Editor
- Lars H. Lindholm

Dear member,

Again it is a pleasure for me and the Hypertension News team to present a new issue - the 39th since we started our electronic newsletter in 2003.

If you want to look at older issues you will find these on the ISH website. From next year, the ISH Communications Committee will have several ways of informing you about ongoing Society matters as well as news from the hypertension field. First, the ISH website, second Hypertension News (with four issues per year), and third a monthly email update from the ISH Secretariat.

The newsletter (Explore) previously circulated by our outstanding New Investigators will now be integrated into Hypertension News. The December New Investigator Committee contribution has been written by Fady Hannah-Shmouni. I would like to take this opportunity to thank Helen Horsfield and her team at the ISH Secretariat for making all this possible. I hope you agree that they are, just great!

In this issue, you will find a report from our President Rhian Touyz informing us about her first half year in office. As you can see, a lot of things have happened in this time and there is a long list of activities soon to come. Of most interest, a new category of ISH membership is under development entitled 'Emerging Leaders'. This will offer an important bridge between the Research Fellow and Regular Member categories.

In Opus 39, Peter W. de Leeuw (Maastricht) and Dylan Burger (Ottowa) cover the 'Hot of the Press' section. They focus on i) Baroreceptor activation therapy and ii) DC isoketal-modified proteins activate T cells and promote hypertension, respectively. We hope you will find these clinical and basic science papers of interest.

Finally, many of you recently lost a good friend. Pieter van Zwieten died on 17 September and he is remembered by John Chalmers and Giuseppe Mancia on page 17. Peter was an outstanding pharmacologist and strongly committed to our Society. He was President of ISH from 1990 to 1992 and of ESH from 1997 to 1999. He was also a wonderful friend and many of us miss him deeply.

Have a good read!

Lars H Lindholm, Editor

Contents

From the ISH President - Rhian Touyz

It is almost 6 months since I assumed the Presidency of ISH and I am delighted to update you on the many activities that have taken place during this time. In the last newsletter you received my vision and goals for ISH. I would now like to share with you how these goals are being addressed and how we are progressing the vision of the Society.

Investing in the next generation of hypertension researchers, with a focus on mentoring. The New Investigator Committee (NIC) has had a very busy period by participating in several symposia linked to major international meetings, including the Council on Hypertension (American Heart Association) Scientific Sessions (San Francisco in September), with future new investigator meetings planned across the globe and to be announced shortly.

The new investigator spotlight feature celebrated its 3-year anniversary in September. This is highlighted in the current issue of Hypertension News and reflects on the incredible growth and success of the NIC (see page 8).

The NIC have posted multiple new videos on the ISH websites (ISHCasts); of the trainee awardees of the San Francisco symposium, and interviews with various Journal editors. These can be viewed at http://ish-world.com/new-investigators-casts/

The NIC Working Groups have been restructured.to include sub-committees focusing on (1) Media (2) Networking and Mentorship and (3) Recruitment. Eleven countries are represented through the 23 NIC and Working Group members.

Mentorship Scheme.
The Mentorship Scheme was re-launched at the Athens ESH-ISH meeting and the Society website has now been updated providing comprehensive information regarding mentoring options for trainees and young researchers. Updated webpages:

ISH Mentorship Scheme

Athens mentors and mentees

Nurturing our future ISH leadership is essential.
To maintain engagement by our young researchers and fellows and to ensure seamless progression to regular membership of the Society, a new category of membership is under development called 'Emerging Leaders'. These members will be nurtured and supported through reduced membership fees and other opportunities and they will hopefully mature as the next generation of ISH leaders. Plans are ongoing and the new category will be launched within the next few months.

Advancing knowledge through workshops and summer schools across the globe.
Expanding the already very successful workshops in Africa and South America, plans are underway to develop summer schools and workshops in India, China and South America for 2015. Unfortunately due to the health risks related to Ebola and other constraints, the seminar planned by Professor Robert Fagard in D.R. Congo, 2015, has had to be cancelled. Hopefully future workshops will be planned under the new Chair of the Africa Regional Advisory Group (RAG), Professor Basden Onwubere.

Highlighted meetings and events supported and/or endorsed by the Society in the coming months are listed below. We hope to announce further information on collaborative efforts with national and regional societies of hypertension and related bodies in due course.

- First Gulf Hypertension Conference. Dubai, UAE
- International Society of Nephrology World Congress, Cape Town, South Africa
- Master Course in Hypertension, Beirut, Lebanon
- Latin American Society of Hypertension and Argentine Society of Hypertension Course for GPs, Tucumán, Argentina
- Russian Antihypertensive League Meeting, III International Congress - From Korotkov to present days
- European Society of Hypertension (ESH) Annual Scientific Meeting, Milan, Italy
- Asian Pacific Conference of Hypertension (APCH), Bali, Indonesia
- Summer School in Asia and Australasia with the Asian Pacific Society of Hypertension and local national societies
- American Heart Association - Council on Hypertension - Scientific Sessions, Washington, USA

Other activities to highlight include:

Improved communications.

A monthly update email will be launched early in 2015 to keep our members more informed regarding ISH activities and news in the field of hypertension – an initiative developed by Professor Neil Poulter and the Communications Committee. All members are encouraged to submit information on activities for dissemination to the ISH membership.

New committee structure.

An updated list of committee members can now be viewed on the ISH website.
http://ish-world.com/about/our-officers-committees.htm

2016 ISH meeting - www.ish2016.org

The next ISH conference will take place in Seoul in 2016. Please diarise the dates and plan to submit your best research to the meeting, which promises to be an outstanding conference.

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

Hypertension Seoul 2016

The 26th Scientific Meeting of the International Society of Hypertension

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

Membership.

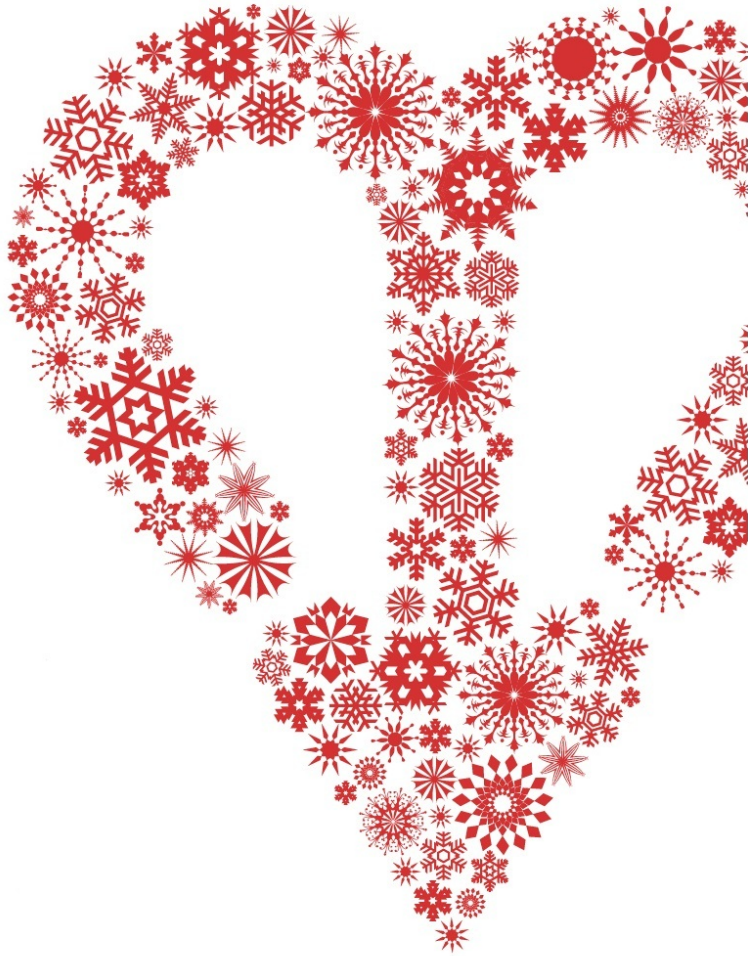
To ensure that you remain connected and that you benefit from being an ISH member, I encourage you to renew your membership by 31st December 2014. Renewal notices have been sent out from the ISH Secretariat office. Also, to ensure growth of the Society, please make every effort to encourage your trainees, fellows and colleagues to become a member.

In summary, you can appreciate that the ISH leadership has been working hard to ensure that your Society serves you in the best possible way. I would like to thank the ISH Executive for their tremendous efforts and dedication over the past few months. Special thanks of appreciation are also extended to Lars Lindholm and his team in preparing Hypertension News, which keeps us all connected, and to Helen, Grace and Jacinta in the Secretariat office, for their superb assistance.

We still have much to do and more goals to reach, but in the meantime, should you have any comments, thoughts or concerns, please let me know by email - secretariat@ish-world.com

Finally, as the Christmas holidays approach and as 2014 comes to a close, I would like to wish you a happy and festive season and all the very best for 2015.

- Rhian Touyz, ISH President



International Society of Hypertension

On behalf of the ISH Leadership, I would like to wish you and your family all the very best for the festive season

Rhian Touyz
ISH President

Hot off the Press

Peter W. de Leeuw

Department of Medicine, Maastricht University Medical Centre Maastricht, The Netherlands

Baroreceptor activation therapy

The regulation of blood pressure involves a variety of mechanisms among which the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS) are the most important ones from a clinical perspective. Drugs targeting the RAAS, for instance, have become a cornerstone in the treatment of hypertension and related conditions such as heart failure. Pharmacological modification of sympathetic activity by means of centrally acting drugs and/or adrenergic receptor blocking agents was very popular once, but today these drugs have lost much of their significance as first-line treatment. Still, the autonomic nervous system remains an attractive target for treatment, particularly in conditions that are associated with enhanced sympathetic activity such as obesity or treatment-resistant hypertension. The latter is defined as a systolic blood pressure ≥140 mmHg despite optimal antihypertensive drug therapy with at least 3 antihypertensive medications including a diuretic. Because patients with resistant hypertension run a high risk of cardiovascular and renal events, there is a need for alternative antihypertensive treatment options in these patients. As such, two device-based techniques, namely renal denervation and baroreceptor activation therapy, have been developed over the past ten years. Both are supposed to reduce sympathetic outflow to the cardiovascular system. Initial results with renal denervation looked extremely promising and as a result this modality gained enormous popularity within a short period of time. However, the recent Symplicity HTN-3 trial has tempered the enthusiasm a bit. Baroreceptor activation therapy (BAT), on the other hand, still seems an attractive way of lowering the pressure.

Although devices for BAT have already been evaluated fifty years ago, it was not until CVRx Inc (Minneapolis, MN, USA) manufactured the Rheos® system that the baroreceptor gained renewed interest as a target for treatment. This novel device consists of an implantable pulse generator (IPG) and two electrodes for implantation at each carotid sinus [1]. The electrical parameters (frequency, amplitude, pulse width) as well as pathway (left, right or bilateral stimulation) can be modulated by an external software program, which connects to the IPG. After initial studies with this device had shown very promising results, a second-generation baropacing system has been developed: the Barostim *neoTM* [2]. It has a much smaller electrode and IPG and it allows for unilateral electrode implantation only. The application of this device has substantially reduced the time needed for the surgical implantation and improved patient tolerability.

An entirely new development in the area of BAT is the mechanical stimulation of the carotid sinus with the MobiusHD*TM* device (Vascular Dynamics, Mountain View, CA, USA). This implant is delivered to the carotid sinus by a catheter in a stent-like fashion and increases the mechanical strain in the carotid area [3]. The results with this device, however, are still too premature to comment on.

The main mechanism, by which BAT is thought to lower blood pressure, is inhibition of sympathetic outflow and enhancement of vagal activity. Clearly, muscle sympathetic nerve activity (MSNA) falls sharply, concurrent with a decline in blood pressure, upon activation of the device and the opposite occurs after it has been switched off. The changes in heart rate variability and heart rate turbulence following a period of BAT are consistent also with inhibition of sympathetic activity and increase of parasympathetic activity. Although it was anticipated that plasma renin levels would fall during BAT, they appear to do so only in animal experiments and not so much in humans. This may be partly explained by the effect of concurrent medication and partly by the fact that greater falls in blood pressure tend to elicit a rise in renin. After the uncontrolled DEBuT trial had shown that the Rheos® system was capable of lowering blood pressure over a long period of time (figure 1), the randomized, double-blind pivotal trial was performed to further assess the safety and efficacy of this device. This trial randomized 265 patients with resistant hypertension from 49 medical centres in a 2:1 fashion to immediate BAT (group A) or deferred BAT (group B). While group A started BAT one month after the implantation procedure, group B started therapy 7 months after the implantation. Although the trial did not meet the endpoint for acute systolic blood pressure response rates at 6 months, it demonstrated that 42% of participants in group A versus 24% of those in group B had a systolic blood pressure ≤140 mmHg after 6 months of follow-up ($p = 0.005$). In addition, long-term follow-up data of this trial showed sustained blood pressure reductions in responders with an average of 35/16 mmHg with 76% clinically significant responders to therapy [4].

The second generation Barosim *neoTM* has essentially shown the same blood pressure lowering as the Rheos® system. Thirty patients (including patients with prior renal denervation) with drug-resistant hypertension were enrolled in an open-label study, in which they received BAT by Barostim *neoTM*. Arterial blood pressure decreased by an average of

26/12 ± 4/3 mmHg after 6 months of therapy [2].

Most serious adverse events (SAE) with the Rheos® system were procedure-related and not device-related. The most prevalent events were transient or permanent nerve injuries. With the Barostim *neoTM* device the safety profile is even better. Long-term BAT safety has improved with the second-generation device from 87% in the Rheos Pivotal Trial to 97% with the Barostim *neoTM* device. Apart from the evident reduction in procedure implant time, less patients receiving the Barostim *neoTM* experience system- or procedure-related events [2].

Although participants from both groups (i.e. immediate as well as deferred BAT) in the Rheos Pivotal Trial showed a mild decrease in estimated glomerular filtration rate (eGFR) six months after the implantation, no further reduction in eGFR was observed with prolonged BAT. This observation suggests that the apparent decline in eGFR was a non-specific phenomenon, perhaps related to the blood pressure reduction [5]. Long-term data about the reduction in lifetime risk of cardiovascular events by BAT are still lacking. In a simulated model, BAT reduced the rates of hypertension-related complications to such an extent that the procedure seemed to be cost-effective compared to optimal drug therapy [6]. However, real-life data from long-term studies are necessary before we can make any firm conclusions on the cost-effectiveness of BAT, especially in younger patients.

What have we learnt so far from our experiences with BAT? First of all, the fact that it produces a sustained fall in blood pressure challenges the time-honored concept of the baroreceptor mechanism being important only for short-term blood pressure control. In addition, recent observations indicate that unilateral stimulation of the carotid area is as effective, if not more, as bilateral stimulation. Comparing left to right shows a somewhat better response with right-sided stimulation [7]. Thus, we also have to rethink our concepts about the symmetry of the baroreceptor system. The most important, however, is that we have managed to treat hypertensive patients who were resistant to a variety of drugs and who now have a somewhat better prognosis.

REFERENCES:

1. Scheffers, I.J., et al., Rheos Baroreflex Hypertension Therapy System to treat resistant hypertension. Expert Rev Med Devices, 2008. 5(1): 33-9.

2.Hoppe, U.C., et al., Minimally invasive system for baroreflex activation therapy chronically lowers blood pressure with pacemaker-like safety profile: results from the Barostim neo trial. JASH, 2012. 6(4): 270-6.

3. Toorop, R.J., et al., Rationale of novel interventions for resistant hypertension. Eur J Vasc Endovasc Surg 2011. 42(5): 557-9.

4. Bisognano, J.D., et al., Baroreflex activation therapy lowers blood pressure in patients with resistant hypertension: results from the double-blind, randomized, placebo-controlled rheos pivotal trial. J Am Coll Cardiol, 2011. 58(7): 765-73.

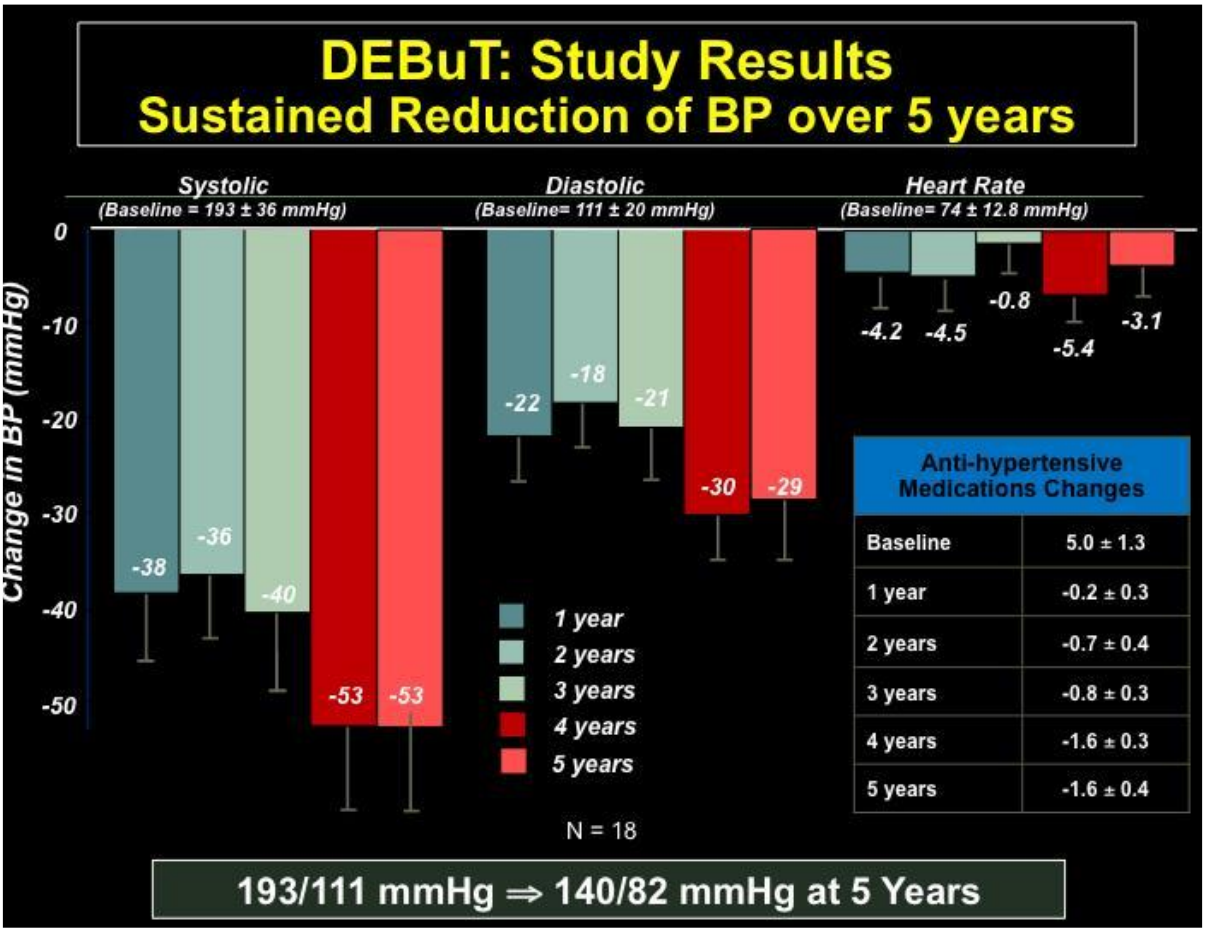
5. Alnima, T., et al., Renal responses to long-term carotid baroreflex activation therapy in patients with drug-resistant hypertension. Hypertension, 2013. 61(6): 1334-9.

6. Borisenko, O., et al., Cost-effectiveness of Barostim therapy for the treatment of resistant hypertension in European settings. Journal of hypertension, 2014. 32(3): p.681-92.

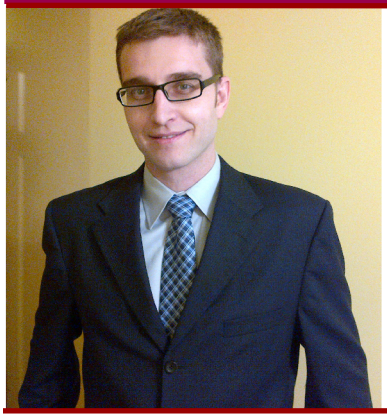
7. de Leeuw, P.W., et al., Bilateral or Unilateral Stimulation for Baroreflex Activation Therapy. Hypertension, 2014, Published online before print October 20, 2014, doi: 10.1161/HYPERTENSIONAHA.114.04492.

- Peter W. de Leeuw

Figure 1



Hot off the Press



Dylan Burger
Ottawa, Canada
New Investigator and Communications Committee Member

DC isoketal-modified proteins activate T cells and promote hypertension

Kirabo *et al.* (2014) *J Clin Invest* guage

For several years there has been intensifying focus on the role of the immune system in hypertension. Preclinical evidence of a link between inflammation, immunity, and hypertension dates back to at least the 1960s, however much of the modern interest in this link stems from the work of David Harrison's laboratory. In particular Guzik *et al.* (2007) [1] showed that mice lacking T- and B-lymphocytes (Rag1-/- mice) fail to develop hypertension in multiple experimental models. Adoptive transfer of effector T-lymphocytes, but not B-lymphocytes restored the hypertensive response. This study highlighted the importance of the adaptive immune system in hypertension and has been consistently reproduced, notably by Crowley *et al.* (2010). [2] The laboratory of Ernesto Schiffrin has also contributed significantly to this area demonstrating an important protective role for T-regulatory lymphocytes, which oppose the actions of T-effector lymphocytes [see Barhoumi *et al.* (2011)]. [3] In a follow-up to their 2007 work the Harrison lab further illustrated the importance of immune activation in hypertension by showing that inhibition of T-cell co-stimulation not only blocked hypertensive responses but also reversed established hypertension in mice [Vinh *et al.* (2010)]. [4] Despite these and other advances, the trigger of inflammatory responses in hypertension has not been clear and this has tempered enthusiasm and limited translational appeal.

In the October issue of the *Journal of Clinical Investigation* Kirabo *et al.* [5] identify a novel mechanism for T-cell activation and development of hypertension. In a series of elegant experiments the authors show that oxidatively modified protein adducts known as isoketals (also known as gamma-ketoaldehydes) accumulate in the dendritic cells of hypertensive mice. The modified dendritic cells in turn, activate T-cell proliferation, and increase T-cell production of inflammatory cytokines. In human studies, serum from patients with resistant hypertension also exhibited elevated isoketal markers. Most convincingly, the administration of isoketal scavengers reduces blood pressure in two mouse models of hypertension (angiotensin II infusion, DOCA-salt) and transfer of isoketal-modified dendritic cells increased blood pressure responses in recipient animals. These data further underscore the importance of the immune system in hypertension and importantly may identify new therapeutic avenues for hypertension.

REFERENCES:

1.Guzik TJ, Hoch NE, Brown KA, McCann LA, Rahman A, Dikalov S, Goronzy J, Weyand C, Harrison DG. Role of the T cell in the genesis of angiotensin II induced hypertension and vascular dysfunction. J Exp Med. 2007 Oct 1;204(10):2449-60.

2. Crowley SD, Song YS, Lin EE, Griffiths R, Kim HS, Ruiz P. Lymphocyte responses exacerbate angiotensin II-dependent hypertension. Am J Physiol Regul Integr Comp Physiol. 2010 Apr;298(4):R1089-97.

3. Barhoumi T, Kasal DA, Li MW, Shbat L, Laurant P, Neves MF, Paradis P, Schiffrin EL. T regulatory lymphocytes prevent angiotensin II-induced hypertension and vascular injury. Hypertension. 2011 Mar;57(3):469-76.

4. Vinh A, Chen W, Blinder Y, Weiss D, Taylor WR, Goronzy JJ, Weyand CM, Harrison DG, Guzik TJ. Inhibition and genetic ablation of the B7/CD28 T-cell costimulation axis prevents experimental hypertension. Circulation. 2010 Dec 14;122(24):2529-37.

5. Kirabo A, Fontana V, de Faria AP, Loperena R, Galindo CL, Wu J, Bikineyeva AT, Dikalov S, Xiao L, Chen W, Saleh MA, Trott DW, Itani HA, Vinh A, Amarnath V, Amarnath K, Guzik TJ, Bernstein KE, Shen XZ, Shyr Y, Chen SC, Mernaugh RL, Laffer CL, Elijovich F, Davies SS, Moreno H, Madhur MS, Roberts J 2nd, Harrison DG. DC isoketal-modified proteins activate T cells and promote hypertension. J Clin Invest. 2014 Oct 1;124(10):4642-56.

- Dylan Burger

Institute Focus

George L. Bakris, MD, F.A.S.N., F.A.S.H., Director
Faculty-Colleen Majewski, MD, Matthew Sorrentino, MD

University of Chicago Medicine/
ASH Comprehensive Hypertension Center

The American Society of Hypertension (ASH) Comprehensive Hypertension Center has a tradition of research, patient consultation and physician education. It was the first center in the United States with this designation. There are now a dozen such centers in the United States. For information about criteria to be such a center go to http://www.ash-us.org/HTN-Specialist/Designated-HTN-Centers/Criteria-for-HTN-Centers.aspx

The Center has been involved in a variety of clinical trials mainly focusing on chronic kidney disease progression associated with diabetes as well as cardiovascular outcome trials in people with kidney disease. Some of the national and international clinical trials in which the center has participated while at the University of Chicago Medicine include, ACCOMPLISH, AASK, SONAR, CREDENCE, AMYTHEST, and SYMPLICITY HTN-3. Since its inception, the Program has been involved in the development and participation of more than two dozen additional trials. Additionally, we have several single center studies focused on pathophysiology of changes in hormone and vascular profile including the EFFORT and ongoing studies evaluation the role of visceral adiposity on aldosterone production in obese peri-menopausal women.

Clinical we have a hypertension consult service for both inpatient and outpatients. We see exclusively referral patients with resistant hypertension usually in the setting of advanced nephropathy and diabetes. The outpatient clinic meets twice weekly. Patient referrals usually come from a 400-mile radius but we have had referrals from Egypt, Europe, India and China. For clinical services, we have a dedicated Hypertension Fellow in addition to a nurse and dietician as well as psychologist.

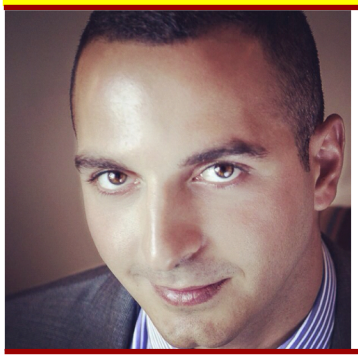
The Hypertension fellowship program at the University of Chicago started in 2006, when I arrived. It is a continuation of the program started at Rush University Medical Center by me in 1993. It is designed to provide expertise in the area of Hypertension and clinical research to people who have completed their general medical training and are either contemplating or are in one of the following medical subspecialties: cardiology, nephrology, endocrinology or general internal medicine. Upon completion of the program, all candidates are board eligible for the Hypertension Boards given by the American Society of Hypertension Specialist Group.

HTN Center

The broad objective of the fellowship is to teach physicians how to initiate, carry out and complete meaningful clinical research studies. The focus of the research will be to understand the consequences of Hypertension as they relate to the genesis of cardiovascular, metabolic (diabetes) and renal disease. Moreover, the fellowship will focus on strategies that may prevent or delay the onset of these problems. To achieve this goal, we have formulated a curriculum that incorporates knowledge and skills from the areas of epidemiology, statistics, and clinical pharmacology. To date, 37 fellows have completed the program and one is currently in the program with another candidate already accepted for the 2015-2016 position. About 33% of the fellows are in academic institutions with about 45% being cardiologists and 40% nephrologists and the remainder endocrinologists or general internists.

- George Bakris

New Investigator Committee (NIC) Update



Fady Hannah-Shmouni, MD

Internal Medicine, Yale-New Haven Hospital
Lead, ISH New Investigator Spotlight

ISH NIC Spotlight Celebrates Third Year

Yale University. New Haven, Connecticut - The ISH New Investigator Spotlight was created in 2011 with the backing and support of the 1st New Investigator Committee (NIC) Chair, Professor Bo Carlberg and ISH President 2010-2012 - Professor Stephen Harrap, with the mission of providing new scientists an opportunity to display their personal and professional qualities for greater visibility on ISH's revamped website. The program has expanded under the current great leadership of Dr. Maciej Tomaszewski (Chair, ISH NIC 2012 to date) to include monthly spotlights from various disciplines, spanning from lab scientists to medical residents. These outstanding scientists, from across the globe, share several important qualities: a passion for cardiovascular research, a tremendous work ethic, and production of quality science.

The monthly *"Spotlight"* is selected based on their scientific achievements and involvement with ISH NIC. Most of our recent Spotlights included individuals who have attended and received recognition at the annual ISH NIC symposium. Members of the Society who are in the early stages of their career (such as graduate students, postdoctoral research fellows or junior faculty members) are encouraged to submit an application for consideration. The applicants are provided with a tailored questionnaire to help highlight their science and future goals. Since its creation, over 25 new profiles have been published, offering a great opportunity for these enthusiastic investigators to connect to the world of hypertension research.

An internal survey was conducted in November of 2014 to study the satisfaction of our Spotlights.

- The majority concluded that our process brings *"exposure to social media"* which is assisting with their research visibility and professional development.
- The majority felt that they were likely to recommend the New Investigator Network to a colleague.
- When asked about their mentor's response, the majority responded, *"the mentor felt very proud"* and that *"the exposure brought about important visibility to their research group"*.

Some of the other comments that we felt very proud of are:

"I find it fascinating to get to know different young researchers, and discover how diverse our Society is"

"The kind of investigators in membership and attending the symposia are diverse and new in the field"

"The keynote address this year was particularly inspiring. Also, the relaxed nature of the entire symposium was a pleasure to be a part of"

From our featured scientist, we have learned valuable lessons. For instance, our November 2014 Spotlight, Mr. McCarthy, who's research is focused on vascular function and innate immune system in hypertension, under the mentorship of Dr. Clinton Webb (Chair, Department of Physiology, Georgia Regents University), advises all scientists to *"keep your eyes peeled for the implicit lessons in science and life; sometimes they're just as valuable as the explicit ones"*. These, amongst other truthful recommendations, have helped our ISH NIC community to foster new relationships between researchers across the globe.

Dr. Veerabhadrappa (Lead, ISH NIC Recruitment Working Group), whose research is focused on vascular inflammatory biomarkers in hypertensive subjects, notes *"the growing interests of our new investigators in joining our initiatives, including the monthly spotlight, is positive for the field of hypertension research. ISH NIC is devoted to helping new scientists feel supported and appreciated"*.

These are some quotes from our most recent Spotlights:

"My long-term career goal is to establish myself as an independent career researcher in the hypertension research field". Dr Lucinda Hilliard – Postdoctoral Research Fellow in the Department of Physiology at Monash University

"It is our mission to conduct dynamic and focused research regarding cardiovascular diseases in various ethnic populations of South Africa in order to have a significant understanding regarding the development of hypertension

and cardiovascular disease." Dr. Carina Mels, Senior Lecturer, Hypertension in Africa Research Team

"My proudest moment was when I received pre-doctoral funding through NIH/NINR." Christina Pettey, Clinical Assistant Professor, University of Arkansas for Medical Sciences

As we continue to recruit exceptional new investigators to lead our New Investigator Spotlight initiative, we hope to expand our mission to include individuals from all scientific disciplines. Stay tuned for 2015's unique lineup.

New Investigators featured since 2011

ISH NIC Spotlight Testimonial

University of Tasmania, Australia

- Sonja Nikolic

*"The ISH New Investigator Network Spotlight is a great initiative of the ISH to create a platform for emerging investigators like me where I could learn about other researchers, their projects and progress at this early career stage. I was particularly honored to be selected as the **September 2013 Spotlight of the Month** and be able to introduce myself to other investigators. I was complimented by my supervisors and other researchers at the Menzies Institute for Medical Research, and it was extremely satisfying to see that my Spotlight profile attracted a lot of attention from other investigators in my research area. I look forward to contributing more to ISH/NIN initiative in the future, as it has provided me a great experience and I am very thankful for this valuable opportunity."*

- Fady Hannah-Shmouni

Follow ISH Society and NIC activites

www.ish-world.com/NIN

www.facebook.com/ISHNIN

www.twitter.com/ISHNIN

From the ISH 2014 Austin Doyle Award Winner

Vikas Kapil, Rayomand S. Khambata, Amy Robertson, Mark J. Caulfield, Amrita Ahluwalia

Hypertension 2014 Nov 24. DOI HYPERTENSIONAHA.114.04675 [Epub ahead of print]

Dietary nitrate to reduce blood pressure lowering in hypertensive patients: a randomized, double-blind, placebo-controlled clinical trial

William Harvey Research Institute, Barts BP Centre of Excellence, NIHR Cardiovascular Biomedical Research Unit at Barts, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London.

Recently enzymatic reduction of *inorganic* nitrate (NO3-), found in large amounts in green-leafy vegetables, to nitrite (NO2-) as an intermediate, and thence to the potent vasodilator nitric oxide (NO) has emerged as a potential pathway that might be exploited as a method for delivery of NO to the blood vessel. Evidence in healthy volunteers suggests nitrite reduction occurs readily within the circulation following elevation of plasma nitrite levels, by provision of dietary or oral inorganic nitrate salts.1 We explored in this phase 2 clinical study whether a once-daily dietary nitrate supplementation for 4 weeks would confer sustained BP reduction in both drug-naïve and treated hypertensive patients.

We randomly assigned 68 hypertensive patients in a double-blind, placebo-controlled clinical trial to receive daily dietary supplementation for 4-weeks with either dietary nitrate (250mL daily, as beetroot juice) or a placebo (250mL daily, as nitrate-free beetroot juice) following a 2-week run-in period and followed by a 2-week wash-out. We performed stratified randomization of drug-naïve (n=34) and treated (n=34) hypertensive patients aged 18-85 years. The primary end-point was change in clinic, ambulatory and home blood pressure compared to placebo.

The intervention was well tolerated and delivered ~6·4mmol nitrate in the 250mL daily dose, which compares to average intake of nitrate from regular food sources of 1.5-2mmol daily.2 Daily supplementation with dietary nitrate was associated with reduction in blood pressure measured by 3 different methods. Mean (95% CI) reduction in clinic blood pressure was 7.7/2.4mmHg (3.6-11-8/0.0-4.9,p<0.001 and p=0.050). 24h ambulatory blood pressure was reduced by 7.7/5.2mmHg (4.1-11.2/2.7-7.7,p<0.001 for both). Home blood pressure was reduced by 8.1/3.8mmHg (3.8-12.4/0.7-6.9,p<0.001 and p<0.01) with no evidence of tachyphylaxis over the 4-week intervention period. Endothelial function, measured by ultrasound flow-mediated dilatation, improved by 1.0% (0.3-1.5,p<0.001) and aortic pulse wave velocity was reduced by 0.59m/s (0.24-0.93,p<0.01) after dietary nitrate consumption with no change after placebo. In pre-specified sub-group analysis, BP was significantly reduced in both drug-naïve and treated hypertensive patients.

This is the first evidence of durable blood pressure reduction with dietary nitrate supplementation, either as monotherapy or in conjunction with conventional pharmacotherapy. The potential importance of our findings is substantial when one considers that each 2 mmHg increase in SBP increases mortality due to ischaemic heart disease and stroke by 7% and 10% respectively.3 Despite more than 60 years of innovation in the pharmacotherapy of hypertension, only ~half of treated hypertensive patients are controlled to guideline-driven targets4 and therefore an additional strategy, based on intake of nitrate-rich vegetables, may prove to be both cost-effective, affordable and favourable for a public health approach to hypertension. These data should spur large-scale, long-term outcome studies to explore the utility of a dietary nitrate-based therapeutics approach to hypertension and cardiovascular risk mitigation.

Funded by The British Heart Foundation, Clinicaltrials.gov: NCT01405898

REFERENCES:

1. Webb AJ, Patel N, Loukogeorgakis S, Okorie M, Aboud Z, Misra S, Rashid R, Miall P, Deanfield J, Benjamin N, MacAllister R, Hobbs AJ, Ahluwalia A. Acute blood pressure lowering, vasoprotective, and antiplatelet properties of dietary nitrate via bioconversion to nitrite. Hypertension. 2008;51:784-790.

2. European Food Standards Agency. Nitrate in vegetables: Scientific opinion of the panel on contaminants in the food chain. EFSA J. 2008;689:1-79.

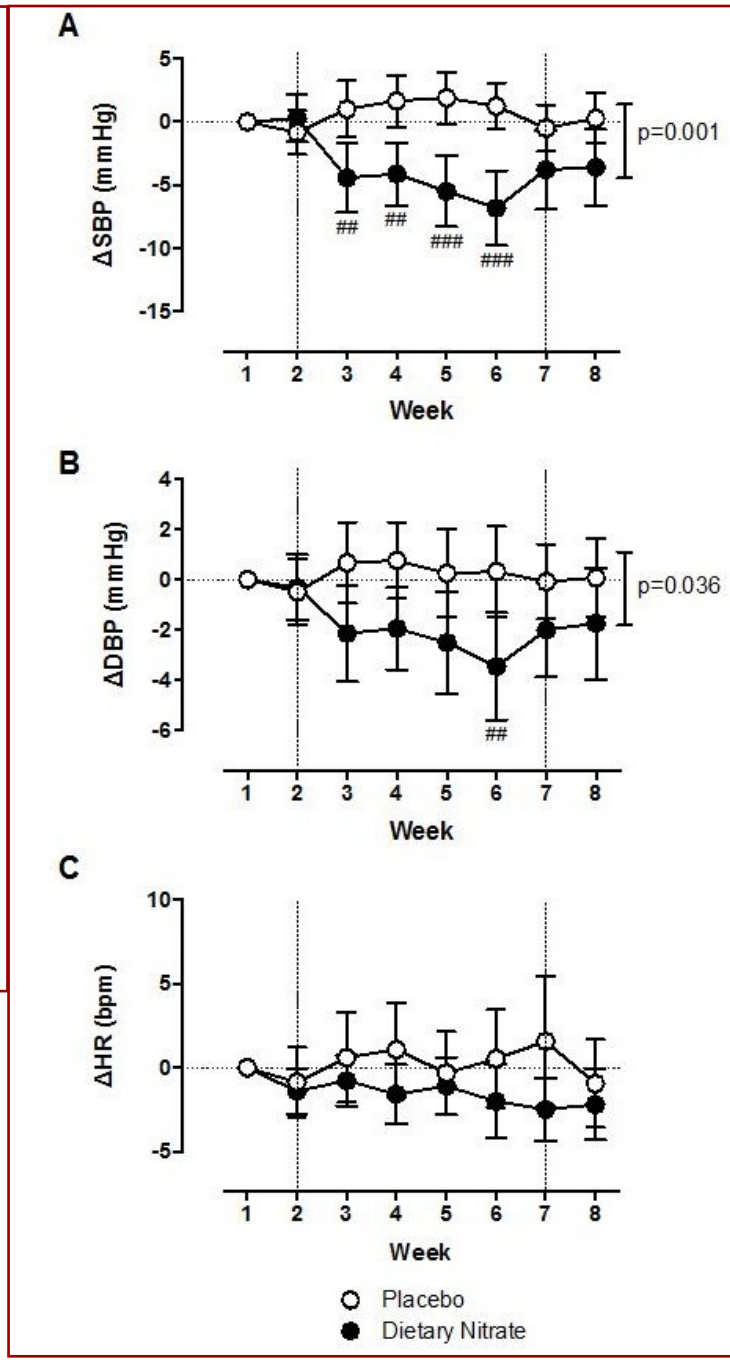
3. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360:1903-1913.

4. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. JAMA. 2010;303:2043-2050.

Figure 1

Dietary nitrate consumption reduces home BP over entire 4 week intervention period in hypertensive patients. The effects of 4 weeks dietary nitrate consumption (beetroot juice 250 mL daily) or placebo (nitrate-depleted beetroot juice 250 mL daily) on change in weekly (A) SBP and (B) DBP and (C) HR from baseline (Week 1) measured at home. Data are expressed as mean±SD. Significance shown for comparisons between treatment allocations for 2-way ANOVA; followed by ##p<0.01 and ###p<0.001 for Bonferroni *post hoc* test. (BP=blood pressure; DBP=diastolic blood pressure; HR=heart rate; SBP=systolic blood pressure). The vertical dotted lines at 2 and 7 weeks signify the end of the 2-week run-in and the beginning of the washout periods.

- Vikas Kapil



Odd Corner

Letter from The Lancet - July, 1885

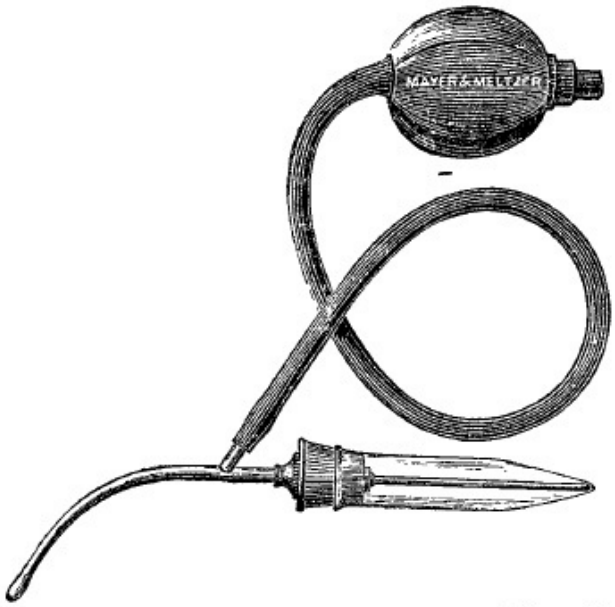
New Inventions.

ANOTHER COCAINE SPRAY-PRODUCER.

THE uses and modes of application of cocaine being very much before the profession just now, I would beg a little space to introduce a cocaine spray-producer which is made by Messrs. Mayer and Meltzer of Great Portland-street. It is on the principle of the ordinary scent-sprays. The jet-tube being single occupies less room than the double one, and there is an advantage in this, especially when treating the nose. The bore of the tube is very minute, and the spray is so fine as to resemble small dust. But the chief advantage of the single bellows is that it ejects the spray instantaneously: there is no delay in "getting up steam," so to speak. I may add that the whole apparatus is small, of a rather elegant appearance, and is very inexpensive.

R. SHALDERS MILLER, M.B., B.S., F.R.C.S.

Windsor, July 10th, 1885.



THE LANCET,] [JULY 25, 1885.

Council's Corner: Hypertension Issues - a personal View

Masatsugu Horiuchi, MD, PhD
Department of Molecular Cardiovascular Biology and Pharmacology
Ehime University, Graduate School of Medicine Ehime, JAPAN

Protective Arm of Renin-Angiotensin System: Possible New Drug Target - from Inhibition to Regulation of Renin-Angiotensin System

The renin-angiotensin system (RAS) plays a role not only in blood pressure regulation, but also in the cardiovascular system. The development of drugs for hypertension and other cardiovascular diseases has been largely dominated by inhibitors of the angiotensin-converting enzyme (ACE)/angiotensin II/angiotensin type 1 (AT1) receptor axis as the classical RAS. Angiotensin II binds two major receptors, the AT1 receptor and type 2 (AT2) receptor. It has been recognized that AT2 receptor activation not only opposes AT1 receptor actions, but also has unique effects beyond inhibitory crosstalk with AT1 receptor signaling. From this point of view, AT2 receptor agonists such as compound 21 have been developed and are expected to be useful agents for improving various pathological disorders. Recent experimental studies have also demonstrated the existence of novel pathways beyond the classical actions of RAS. Angiotensin-(1-7) is produced from angiotensin I or angiotensin II by the catalytic activity of angiotensin-converting enzyme 2 (ACE2), and the Mas receptor has been identified as the binding protein mediating the inhibitory actions of angiotensin-(1–7) on angiotensin II-mediated AT1 receptor actions. A new axis of RAS, the ACE2/angiotensin-(1-7)/Mas axis, has been highlighted as the counteracting partner of the ACE/angiotensin II/AT1 receptor. Moreover, it is reported that angiotensin-(1-7) can act as an endogenous ligand with AT2 receptor selectivity over the AT1 receptor. These results support the concept that interruption of crosstalk of various angiotensin receptors could determine and orient pathological states, resulting in the onset of cardiovascular diseases. Moreover, angiotensin II mediates various effects through complex signaling pathways on binding to its G-protein-coupled receptors (GPCRs), the AT1 receptor and AT2 receptor. These receptors are regulated by GPCR-interacting proteins such as AT1 receptor-associated protein (ATRAP), ARAP1 (AT1 receptor associated protein) and AT2 receptor-interacting protein (ATIP).

The newly discovered angiotensin-(1–12), which is cleaved from angiotensinogen by a yet-to-be-defined non-renin enzyme, is converted to angiotensin II largely by chymase, and numerous studies have suggested that there exist other proteases capable of cleaving angiotensin substrate. Other angiotensin peptides such as angiotensin A and alamandine are attributable to substitution of aspartic acid with alanine in position 1. The new peptide alamandine differs from angiotensin-(1–7) only by the presence of an alanine residue. Another intriguing finding of the present investigation is the connection of alamandine to the family of Mas-related G-protein–coupled receptors (MrgD).

Further elucidation of the regulatory mechanisms of the functions of RAS beyond the classical ACE/angiotensin II/AT1 receptor axis could provide possibilities for the development of novel drugs that regulate RAS in a more sophisticated manner rather than inhibiting RAS, thereby treating hypertensive patients and achieving cardiovascular risk reduction more efficiently.

REFERENCES;
Dell'Italia LJ, Ferrario CM. The never-ending story of angiotensin peptides: beyond angiotensin I and II. Circ Res. 2013; 112: 1086-7.
Horiuchi M, Iwanami J, Mogi M. Regulation of angiotensin II receptors beyond the classical pathway. Clin Sci (Lond). 2012; 123: 193-203. Sumners C, Horiuchi M, Widdop RE, McCarthy C, Unger T, Steckelings UM. Protective arms of the renin-angiotensin-system in neurological disease. Clin Exp Pharmacol Physiol. 2013; 40: 580-8.
Unger T. Decade in review - hypertension: The past decade in hypertension - facts, hopes, and hypes. Nat Rev Cardiol. 2014 Sep 2. doi: 10.1038/nrcardio.2014.131. [Epub ahead of print]

- Masatsugu Horiuchi

Council's Corner: Hypertension Issues - a personal View

Yoshihiro Kokubo, MD, PhD, F.A.C.C., F.A.H.A., F.E.S.C., F.E.S.O., F.J.S.H.

Department of Preventive Cardiology, National Cerebral and Cardiovascular Center, Suita, Japan

Population-based prospective studies on the combined impact of blood pressure and risk factors on cardiovascular disease

Recently guidelines have been revised and are popular in many areas of medicine. The points of the lifestyle improvement for these guidelines can be summarized in the following: healthy diet (consume a diet rich in fruits/vegetables and low-fat food or fish with a reduced content of saturated and total fat), sodium restriction, weight reduction, regular exercise, moderate alcohol consumption, and smoking cessation. These lifestyle modifications are universal constituents of the major guidelines, which are very similar to the European and the American stroke guidelines.[1] In the European and Japanese guidelines, hypertensive patients are stratified into groups on the basis of their hypertensive levels and primary risk factors. In Japan, however, this stratification is not substantiated by enough evidence. I focused on the evidence concerning the cardiovascular disease (CVD) risks for the combination of blood pressure (BP) categories and other risks in the Suita Study, which is an urban cohort study in a Japanese population. The Suita Study has demonstrated that high-normal BP is a risk factor for incident CVD.[2] An increased risk of CVD was observed in the subjects with impaired fasting glucose and prehypertension, which is equivalent to approximately 10% of the adult population.[3] Chronic kidney disease increases the association of BP and CVD.[4] The number of metabolic syndrome components (i.e., modified NCEP-ATPIII criteria) is more strongly associated with CVD incidence than essential abdominal obesity criterion (the Japanese criterion).[5] The combination of smoking and metabolic syndrome exacerbates the risk of CVD. Lifestyle modification not only for preventing or combating metabolic syndrome but also toward reducing smoking continues to be important as these contribute significantly to CVD.[6] The risk of CVD and its subtypes was consistently higher in the hypertensive participants than in the non-drinkers without hypertension, irrespective of alcohol consumption.[7] Recently, I have reviewed a manuscript concerning the prevention of hypertension and CVD, that compared lifestyle factors in Westerners and East Asians, and mentioned the old saying "taking a lesson from the past".[8] This review concluded that, to prevent high BP, East Asians should pay particular attention to quitting smoking and reducing salt and alcohol intake, whereas Westerners need to pay closer attention to weight control, including regular exercise, and consider replacing dietary meat high in saturated fat with fish. Among Japanese, the high alcohol intake and high rate of aldehyde dehydrogenase deficiency, in addition to high salt intake and high rate of salt sensitivity, may contribute to their elevated BP. I continue to study hypertension areas and I hope to contribute to further progress in preventive medicine, particularly regarding CVD.

REFERENCES:

1. Kokubo Y. Traditional risk factor management for stroke: a never-ending challenge for health behaviors of diet and physical activity. Curr Opin Neurol.2012;25:11-17.

2. Kokubo Y, et al. Impact of high-normal blood pressure on the risk of cardiovascular disease in a Japanese urban cohort: the Suita study. Hypertension.2008;52:652-659.

3. Kokubo Y, et al. The combined impact of blood pressure category and glucose abnormality on the incidence of cardiovascular diseases in a Japanese urban cohort: the Suita Study. Hypertens Res.2010;33:1238-1243.

4. Kokubo Y, et al. Relationship between blood pressure category and incidence of stroke and myocardial infarction in an urban Japanese population with and without chronic kidney disease: the Suita Study. Stroke.2009;40:2674-2679.

5. Kokubo Y, et al. Impact of Metabolic Syndrome Components on Incidence of Cardiovascular Disease in a General Urban Japanese Population: the Suita Study Hypertens Res.2008.

6. Higashiyama A, et al. Risk of smoking and metabolic syndrome for incidence of cardiovascular disease--comparison of relative contribution in urban Japanese population: the Suita study. Circ J.2009;73:2258-2263.

7. Higashiyama A, et al. Alcohol consumption and cardiovascular disease incidence in men with and without hypertension: the Suita study. Hypertens Res.2013;36:58-64.

8. Kokubo Y. Prevention of Hypertension and Cardiovascular Diseases: A Comparison of Lifestyle Factors in Westerners and East Asians. Hypertension.2014;63:655-660.

- Yoshihiro Kokubo

Council's Corner: Hypertension Issues - a personal View

Dorairaj Prabhakaran

Vice President, Public Health Foundation of India and Executive Director, Centre for Chronic Disease Control, New Delhi, India

Hypertension in India – a growing challenge that requires a comprehensive response

Currently non-communicable diseases (NCDs) such as cardiovascular diseases (CVD), diabetes, chronic lung diseases and cancers are the principal cause of morbidity, mortality and disability in India. As a result on ongoing health transitions, India faces the dual burden of diseases – a scenario in which infectious diseases, maternal and child health issues remain a considerable challenge along with the rising burden of NCDs.

According to the Global Burden of Disease estimates, the fourth foremost preventable NCD risk factor in India today is hypertension or high blood pressure.1 Projections indicate that the number of hypertensives in India will nearly double from 118 million in 2000 to 213 million by 2025. Hypertension is estimated to be responsible for nearly 10% of all deaths. Hypertension prevalence in adults has risen dramatically across India over the past three decades from about 5% in certain rural and urban communities to between 20%-40% in urban areas and 12%-17% in rural areas. Many more have pre-hypertension, which underlines the fact that a comprehensive response is required. Between 1942 and 1997, the mean systolic blood pressure (SBP) had also increased from 120 mmHg to 130 mmHg, particularly among 40 to 49 year old urban men. National trend data are unavailable, but many sub-national studies have reported increases in hypertension across the country over the past two decades in consonance with the rapid health transitions that are occurring, resulting in altering the way individuals live, work, eat and move. 2

Notably, unlike in developed countries, most of the CVD and hypertension related deaths occur at younger ages with consequent adverse health, economic and societal implications. In 2004 the annual income loss from NCDs among working adults in India was US$ 50 billion and that due to hypertension alone amounted to US$. 860 million.3 Hypertension was also a leading cause for hospitalizations and outpatient visits. The Indian Council of Medical Research (ICMR) estimates that 16% of ischemic heart disease, 21% of peripheral vascular disease, 24% of acute myocardial infarctions and 29% of strokes in India could be attributable to high blood pressure underlining the huge impact effective hypertension prevention and control can have on reducing the rising burden of CVD and NCD.2

Although the burden of hypertension is high, it is inadequately detected and managed. Reports from various parts of India indicate that only about 30% of people with hypertension are detected, less than half of those diagnosed receive anti-hypertensives and only half of them have their blood pressure treated and controlled to recomended targets leading to a huge burden of premature avoidable morbidity, disability and mortality. 2 Though national data on treatment and control are unavailable, sample studies conducted across various regions of India such as North (Delhi 10.5%), South (Chennai 7.5%, Trivandrum 8.6%), East (Assam 18.1%), and West (Mumbai 13.6%) indicate sub-optimal control blood pressure control.4 Inadequate access to health services and simple evidence-based medications, delays in diagnosis, limited opportunistic or targeted screening programmes, poor adherence to prescribed pharmacological and non-pharmacological therapies, and complexities associated with taking multiple medications are some of the reasons for inadequate control and failure to attain treatment targets. Of note, the capacity of the health system to identify those with hypertension, provide appropriate evidence-based interventions and ensure compliance to these interventions is severely limited by a lack of physicians and the high costs of medical treatment.

Considering this increasing disease burden as well as the social, developmental and economic threat posed by NCDs and hypertension, the Government of India has initiated the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS). Its components include: (i) establishment/strengthening of health infrastructure; (ii) early diagnosis and treatment; (iii) human resource development; (iv) health promotion; and (v) monitoring, surveillance and research. The NPCDCS is expected to be integrated into the health system. It has hypertension as a key focus area, as it is easily diagnosable and treatable with lifestyle modification measures and effective medicines, besides providing an entry point to deal with other NCDs as any intervention will help concomitantly

address complications/comorbidities. The programme also entails opportunistic screening for hypertension at the sub-centre level and NCD clinics, as well as training for medical officers and health workers.5

Effectively addressing hypertension in India requires not only strengthening the health system and improving healthcare delivery but also implementation of population based risk reduction strategies. Policies aimed at modest reductions in salt intake/fat intake/sugar intake, increase in physical activity/fruit-vegetable intake and avoiding tobacco use) could prevent a large proportion of disease events in the whole population and complement improvements in healthcare delivery. For example, a 2% population-wide decrease of diastolic blood pressure, such as that easily achievable by modest salt reduction, was estimated to avert 300000 coronary heart disease and stroke deaths in India, with further decreases in blood pressure yielding higher.6 Recent mathematical modelling by Basu et al also suggests that modest salt reduction could substantially reduce cardiovascular disease throughout India. Future myocardial infarctions and strokes in India were predicted with a Markov model simulating men and women aged 40 to 69 years in both urban and rural locations, incorporating the risk reduction from lower salt intake. If salt intake does not change, the authors expect approximately 8.3 million myocardial infarctions (MIs), 830,000 strokes and 2.0 million associated deaths per year among Indian adults aged 40 to 69 years over the next three decades. Reducing intake by 3 g/day over 30 years (−0.1 g/year, 25% reduction) would reduce annual MIs by 350,000, strokes by 48,000 and deaths by 81,000 among this group without producing iodine deficiency. 7

Given the high population salt with the average intake being 9–12 g/day, salt reduction is potentially one of the most cost-effective strategies to prevent hypertension in India and has the additional potential to improve hypertension control rates, reduce the need for anti-hypertensive medications and consequently curb associated health care costs as observed in other countries.8

The escalating burden as well as the low levels of awareness, treatment and control rates of hypertension in comparison to rest of the world warrants priority public health action for prevention and control that incorporates both the high risk and population approaches. This is essential to achieve the United Nations-WHO goal of 25% reduction in premature NCD mortality and associated reductions in hypertension.

REFERENCES:

1.Global Burden of Disease Study, India profile 2013. Available at:
http://www.healthdata.org/sites/default/files/files/country_profiles/GBD/ihme_gbd_country_report_india.pdf
2.Mohan S, Koller T. Hypertension and related comorbidities in India: Implications for the health system. New Delhi, WHO Country Office for India, 2013.
3. Mahal A, Karan A, Engelgau M. The Economic Implications of Non-Communicable Disease for India. Produced by the Health, Nutrition, and Population Family (HNP) of the World Bank's Human Development Network. Washington, D.C, 2010.
4. Devi P et al. Prevalence, risk factors and awareness of hypertension in India: a systematic review. J Hum Hypertens 2012;27:281-87.
5. Ministry of Health and Family Welfare. National programme for prevention and control of cancer, diabetes, cardiovascular diseases and stroke (NPCDCS), Operational Guidelines. Directorate General Of Health Services, Government of India, 2011.
6. Rodgers A, Lawes C, MacMahon S. Reducing the global burden of blood pressure related cardiovascular disease. J Hypertens Suppl 2000; 18: S3–S6.
7. Basu S et al. Dietary Salt Reduction and Cardiovascular Disease Rates in India: A Mathematical Model. PLOS One 2012; 7:e44037. doi: 10.1371/journal.pone.0044037.
8. Mohan S, Prabhakaran D, Krishnan A. Promoting population-wide salt reduction in South East Asia Region: current status and future directions. Regional Health Forum 2013; 17:72-79.

With special thanks to Sailesh Mohan
Senior Research Scientist and Associate Professor,
Public Health Foundation of India, New Delhi, India

- Dorairaj Prabhakaran

Future ISH Biennial Scientific Meetings

2016 **Seoul, Korea**

24-29 September 2016

www.ish2016.org

2018 **Beijing, China**

2020 **Glasgow, UK**

World Hypertension League
- A comment on recent highlighted salt papers

Daniel Lackland
President Elect **WHL** &
Editor, **WHL** Newsletter

Research Studies and Dietary Sodium: A Perspective from the World Hypertension League (WHL)

In an earlier edition of the Newsletter, we summarized the focused session on the current issues regarding dietary salt with effects on blood pressure levels and hypertension-related high blood pressure and hypertension held during the 2014 joint Scientific Meetings of the European Society of Hypertension (ESH) and the ISH in Athens, Greece. The session indicated that the recommendations of salt intake are confused with low-quality studies that include flawed and invalid measures of sodium consumption. Specifically, the session faculty reported that the use of spot urine analyses represents an inaccurate and inappropriate means of estimating sodium consumption. 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. Since the session, there have been two recent New England Journal of Medicine (NEJM) publications relating to dietary sodium. The first study reported that sodium intake <3000 mg /day was associated with an increase in mortality and cardiovascular disease while confirming the health risks of dietary sodium >6000 mg/day (1). The accompanying paper largely confirmed the association between sodium intake and increased blood pressure but, unlike rigorous randomized controlled trials, found less of an impact of sodium intake <3000 mg/day on blood pressure (2). Both studies confirmed that lower dietary potassium is associated with both increased blood pressure and adverse health outcomes. The studies were based on the PURE cohort of over 100,000 people in 17 countries. These reports with associated commentaries prompted a response article from the Executive of the World Hypertension League (3). In this article, the authors reiterate concerns about the weak research methodology in assessing dietary sodium used in the PURE study. Specifically, a single spot urine sample (first or second morning void) was used to estimate a person's sodium intake and single spot urine samples simply are not a reliable method of sodium intake. While the PURE study did attempt to validate spot urine sodium to 24 hr. urine sodium, there are concerns about quality control and completeness of the assessment (3) Likewise, single 24 hr urine samples are not a reliable estimate of usual salt intake as salt intake generally varies day to day in many settings (3).

The American Heart Association has also critiqued the PURE publication in NEJM indicating other methodological weaknesses such as reverse causality whereby sick people eat less salt rather than lower salt consumption causing illness (4). While the PURE study excluded individuals with a history of cardiovascular disease, diabetes, and cancer in an effort to address reverse causality, individuals with potentially high risk for an event such as those with prehypertension, family history, and health screenings of high risk were included in the study (3). Thus, the correlation from the PURE results should be interpreted cautiously because it might be a result of reverse causation.

The WHL and ISH are committed to regular reviews of the literature, the setting of minimum standards for research methods and regular updates to dietary recommendations (5). While the basis for the findings of the PURE study on sodium are unclear, studies based on flawed methodologies are likely to continue to generate controversy and the scientific area will only be advanced by carefully conducted rigorous research (3).

REFERENCES:

1) O'Donnell MJ, Mente A, Rangarajan S, et al. Urinary sodium and potassium excretion, mortality, and cardiovascular events. N Engl J Med 2014;371:612-623

2) Mente A, O'Donnell MJ, Rangarajan S, et al. Association of urinary sodium and potassium excretion with blood pressure. N Engl J Med 2014;371:601-611

3) Campbell, NRC, Lackland, DT, Niebylski, ML and Nilsson, PM. Is Reducing Dietary Sodium Controversial? Is It the Conduct of Studies With Flawed Research Methods That Is Controversial? A Perspective From the World Hypertension League Executive. J Clin Hypertens (Greenwich). 2014. doi: 10.1111/jch.12437

4) American Heart Association, http://newsroom.heart.org/news/excessive-sodium-consumption-has-dire-impact-on-global-health-new-study-finds, accessed Nov 24 2014

5) Campbell N, Niebylski M, Lackland D et al. High Blood Pressure: Why Prevention and Control are Urgent and Important. A 2014 Fact Sheet from the World Hypertension League and the International Society of Hypertension. J Clin Hypertension. 2014 16; 551-553 DOI: 10.1111/jch.12372

- Daniel Lackland

World Hypertension Day – 17th May 2015

The WHD (an initiative of the WHL) was first inaugurated in May 2005 and has become an annual event ever since. The purpose of the WHD is to promote public awareness of hypertension and to encourage citizens of all countries to prevent and control this silent killer, the modern epidemic.

WORLD HYPERTENSION DAY

Initiated by the World Hypertension League

Plan now to mark this special day.

View **www.worldhypertensionleague.org** for further information.

Download and use ISH WHD Posters View ISH WHD videos

~~ In Memoriam ~~

Pieter van Zwieten

20 May 1937 – 17 September 2014

Pieter van Zwieten was an outstanding pharmacologist and a great servant of the International Society of Hypertension. Pieter was Professor and Head of the Department of Pharmacotherapy at the Academic hospital of the University of Amsterdam for many years, and also headed sections of the departments of cardiology and cardio-thorasic surgery at the Academic Medical Centre. He was Dean of the Faculty of Pharmacy at the University of Amsterdam from 1972 to 1985. His research focussed on cardiovascular pharmacology, especially anti-hypertensive drugs and he made important contributions to the mode of action of sympatholytic drugs, alpha blockers, calcium channel blockers and inhibitors of the renin angiotensin system.

Pieter was strongly committed to the International Society of Hypertension and served on its Council for many years, becoming President from 1990 to 1992. He was also a strong servant of the European Society of Hypertension, which has established the Pieter van Zwieten Award for the clinical pharmacology of drugs acting on the renin angiotensin system, in his honour, and he was its President from 1997 to 1999. He travelled extensively as an ambassador of our Society and was made an honorary life member of many national and regional Societies around the world.

Pieter was recognised through invitations to give keynote lectures at many congresses of Pharmacology, of Cardiovascular Diseases and of Hypertension and was the recipient of numerous prestigious awards. Behind an awkward and brusque exterior, Pieter hid a warm heart, an engaging personality, and a wide range of interests. He was also a wonderful mentor and supervisor of many students and research fellows. Through his travels, he was able to maintain active contact with many of the doctoral students he mentored, more than 70 over his career. His presence in our midst will be sorely missed by colleagues and friends in all continents around the world.

- John Chalmers and Giuseppe Mancia

Hypertension Seoul 2016

The 26th Scientific Meeting of the International Society of Hypertension

in collaboration with the 12th 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 **www.ish2016.org**

Theme

"Working together for better BP control and CVD reduction"

Important Dates

Opening of Abstract Submission	September 24, 2015
Abstract Submission Deadline	February 24, 2016
Notification of Acceptance	April 25, 2016
Opening of Online Registration	September 24, 2015
Early Bird Registration Deadline	May 16, 2016
Pre-Registration Deadline	July 31, 2016

Hypertension Seoul 2016
InSession International Convention Service, Inc.
4F Yoongjeon Bldg., 829-6 Yeoksam-dong, Gangnam-gu, Seoul 135-936, Korea
Phone. +82-2-3452-7260, +82-2-3471-8555 Fax. +82-2-521-8683
E-mail. ish2016@insession.co.kr

ISH Corporate Members

The ISH would like to acknowledge the support of our Corporate Members.

Daiichi-Sankyo

SERVIER

astellas

OMRON

Takeda

Mitsubishi Tanabe Pharma Corporation

International Society of Hypertension
Secretariat
c/o The Conference Collective

Email: secretariat@ish-world.com
Website: www.ish-world.com

The opinions expressed by contributors in this issue of Hypertension News do not necessarily reflect or represent the opinions or policy positions of ISH or its Council of Trustees.

Membership Information

ISH Secretariat Contact Details

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

ISH Secretariat

The Conference Collective
Delivering Excellence in Event Management

c/o The Conference Collective

8 Waldegrave Road

Teddington

Middlesex

TW11 8GT

Tel (UK): +44 20 8977 7997
Email: secretariat@ish-world.com

ISH Registered Charity No: 1122135

Membership Subscriptions 2015

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 for 2015 and are interested in retaining your links to the Society, we would be delighted to receive your payment.

Please contact the Secretariat for more information.

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 membership@ish-world.com with any questions.