



Notes from the Editor

- Lars H. Lindholm

The ISH members should be the ones best briefed!



Dear member,

The Communications Committee has decided to upgrade its service to our members, hoping that you will find yourselves "the best briefed on high blood pressure issues".

Hypertension News will be published four times per year, as before, and I will continue to edit it. There will, however, be a stronger focus on more comprehensive contributions. The new "Hypertension e-Bulletin" will be a one or two pager which will be sent to you eight times per year in the months when we don't publish Hypertension News. It will be edited by Neil Poulter. The e-Bulletin will contain short messages or "News" on hypertension which we hope you will appreciate. Both publications rely on the brilliant Helen Horsfield to carry out the editorial work.

The Communications Committee has also decided to take a look at who opens and who does not open Hypertension News. About half of our members open the email, which is a very good rate according to friends in industry. We have very few returns so the email addresses are correct. Moreover, we know that you can get access to Hypertension News in several ways, e.g. by our email, downloading it from the ISH website and in communications from national hypertension societies. We will start with a pilot study of a small group of members to see if it is the same people every time who waive opening the Newsletter. In a second step, we will try to find out why they didn't open it and what we can do to change that.

Enclosed, please find the latest issue of Hypertension News (Opus 40) which I hope you will enjoy. I would like to focus your attention on two contributions i) Gender Aspects in Hypertension Treatment by Karin Manhem and Charlotta Ljungman, with a commentary by Neil Poulter and ii) the contribution on the Georges Pompidou European Hospital Hypertension Excellence Center by Stéphane Laurent.

Have a good read!

Lars H Lindholm, Editor

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From the ISH President - Rhian Touyz



I am delighted to report on recent activities in ISH and to give you an update of new initiatives and plans.

Membership

The membership of our Society continues to grow and I am happy to say that not only is our membership becoming more global, but we are also attracting many more young researchers and fellows. We are also very fortunate in that our Corporate Membership is strong, with ten committed members. **I would like to sincerely thank all our industry supporters.**

ISH 2016 Seoul meeting

We are beginning to plan the **ISH Seoul 2016 Scientific Meeting** with the local organizing committee in Korea and I encourage you all to **'reserve the date'** - **24 - 29 September 2016**. I would like to congratulate Professor Cheol-Ho Kim as the new President of the Seoul 2016 meeting and look forward to working closely with him and his committee in helping to create an outstanding scientific program.

Hypertension Seoul 2016

The 26th Scientific Meeting of the International Society of Hypertension

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



IMPORTANT DATES:

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

Regional Activities

The Regional Advisory Groups (RAGs) have been busy planning activities for 2015.

In particular, the **Africa** RAG is exploring possibilities of a Teaching Seminar in Tunisia. ISH is also exploring opportunities to engage in the Healthy Heart Africa program, sponsored by AstraZeneca.

In **Asia**, ISH faculty will participate in the annual Asian Pacific Society of Hypertension meeting in Bali, and the 2015 China Summer School will be held in the vicinity of Beijing from 3 - 7 August. I am delighted to say that for the first time, in addition to sponsoring senior ISH faculty to participate in the China Hypertension Summer School, we will be sponsoring attendance of members from the New Investigator Committee (NIC), namely Sofie Brouwers and Fadi Charchar.

In **Latin America**, ISH faculty will participate in the Brazilian Hypertension Society and the Latin American Society of Hypertension (LASH) and Argentina Arterial Hypertension Society (SAHA) meetings later in the year.

In the **Middle East and Eastern Europe**, ISH has planned interactions at the following events - (1) Russian Society on Hypertension Conference on Arterial Hypertension (2) Master Course in Hypertension, Electrolytes and the Kidney (3) Russian Antihypertensive League event - III International Congress - From Korotkov to Present Days.

In **North America**, ISH continues to engage with the American Heart Association's Council on Hypertension through networking between the young investigators.

These interactions highlight just a few of the many regional activities of our Society in 2015 and truly represent the global mandate of ISH.

New Initiatives

In addition to the RAG activities, I am delighted to inform you of two new ISH initiatives. Firstly, we will be creating a committee on **'Women in Hypertension Research'**, which will focus on developing programs, mentoring schemes, networking systems etc to support and encourage women in hypertension research. Secondly, ISH will become more actively involved in **'hypertension education'** and as such a committee to oversee the education portfolio will be established. Further information of these exciting activities will be detailed in future newsletters.

World Hypertension League / World Hypertension Day

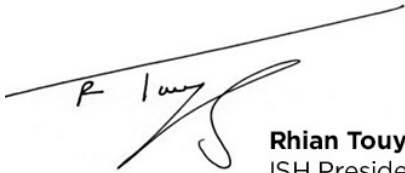
Finally ISH is working closely with the World Hypertension

League (WHL) to promote global awareness of hypertension. In relation to this, ISH will promote World Hypertension Day through a number of programs linked to the WHL. **Please remember the date: 17th May.** All national and regional hypertension organisations are strongly encouraged to promote hypertension awareness in their local regions. Further details will be sent to you from the ISH Secretariat and are also available on the website.

WORLD HYPERTENSION DAY

Initiated by the World Hypertension League

For those of you who will be at the ESH Annual Meeting in Milan, please come by the ISH booth – it would be a pleasure to see you and to share with you the latest ISH news.



Rhian Touyz
ISH President

Hot off the Press



Lars H. Lindholm

**Renal denervation –
again a topic to
discuss!**

Over the past decade, there has been great enthusiasm for the use of renal denervation as a method of achieving blood pressure control when conventional blood pressure lowering drugs have failed.

The target group has been patients with resistant hypertension, defined as blood pressure remaining above goal (often 140/90 mm Hg, lower in diabetics) in spite of three blood pressure lowering drugs of different classes. One of these should be a diuretic and all drugs should be

prescribed in optimal dosages. Last year, Symplicity HTN-3 was stopped prematurely because the trial failed to meet its primary end point based on the change in office blood pressure from baseline to six months. The myth that renal denervation is a magic cure for resistant hypertension has since then disappeared. Instead - as pointed out recently in Hypertension News by Professor Peter Sever and others - we are searching for well controlled trials of renal denervation which are independently sponsored and include optimisation of drug treatment including spironolactone before randomisation as well as urine drug analyses during the trial. Like Symplicity HTN-3 these trials should be SHAM controlled, and ambulatory blood pressure recordings should be used to minimize office-hypertension. If possible, the degree of denervation should also be assessed.

The DENERHTN trial (Optimum and stepped care standardised antihypertension treatment with or without renal denervation for resistant hypertension)

This new trial, recently reported in The Lancet ([click here](#)), is a prospective, randomised, open-label trial with a blinded end-point evaluation. Funding came from the French Ministry of Health. Patients with resistant hypertension were randomised to renal denervation + stepped care drug treatment or to stepped care drug treatment alone. Spironolactone was part of the treatment but after randomisation. Primary endpoint was the change in systolic ambulatory blood pressure from baseline to six month. In all, 106 patients, 62% men, 78% Caucasian, were randomised out of 1416 referred for resistant hypertension. 101 patients were included in the intention-to-treat analyses. The mean change in daytime systolic blood pressure was -15.8 mm Hg in those denervated and -9.9 mm Hg in the others, a base-line adjusted difference of about 5.9 mm Hg (-11.3 to -0.5 mm Hg, $p=0.03$).

The study is carefully designed and very well carried out. It is certainly a difficult trial to undertake. Ambulatory blood pressure recordings have been used which is the best way to follow blood pressure and the study is prospective, randomised with a blinded end point committee - all good! However, there were no SHAM operations. Moreover the drug adherence is based on self reporting and not on drug analyses in urine.

I guess, that these findings will make those who are believers in renal denervation a little happier - at least for a while, and those who have given up on renal denervation will say that it has been shown before (maybe not as elegantly) that renal denervation works in some patients and not in others.

Readers: take a for look yourselves! It is certainly a paper worth reading!

- Lars H. Lindholm



Thomas Kahan

Karolinska Institutet, Department of Clinical Sciences, Danderyd Hospital, Division of Cardiovascular Medicine, Stockholm, Sweden; and Department of Cardiology, Danderyd University Hospital Corporation, Stockholm, Sweden

Left ventricular geometry in hypertensive and prognosis

Signs of hypertensive heart disease are early and important findings with pathophysiological implications in the progression from early hypertension to cardiovascular morbidity and mortality. The important determinants for the development of left ventricular (LV) hypertrophy are hemodynamic factors (such as blood pressure, large artery structure and stiffness, and volume load) and non-hemodynamic mechanisms (such as trophic factors mediated by the sympathetic nervous system, the renin-angiotensin-aldosterone system, and other neurohormonal mediators) [1].

An elevated blood pressure will promote coronary artery atherosclerosis and, together with cardiac hypertrophy, cause myocardial ischemia in hypertensive patients. Also important, an increased afterload will induce cardiomyocyte hypertrophy, stimulate fibroblasts and increase collagen formation, and cause remodelling of the myocardium with an increase in myocardial fibrosis. This will impair systolic contractility and diastolic filling, causing LV systolic and diastolic dysfunction. Myocardial fibrosis will contribute to impaired coronary flow reserve and diastolic dysfunction, and will alter electrical conduction properties and increase the risk for arrhythmias [2,3].

The prognostic value of LV hypertrophy is well established. By use of echocardiography four distinct LV geometrical patterns have been described: Normal LV geometry and mass, LV remodelling (with increased relative wall thickness and normal LV mass), eccentric LV hypertrophy, and concentric LV hypertrophy [4]. It appears that cardiovascular morbidity and all cause mortality associate to the geometric pattern and is lowest in patients with normal LV geometry, and progressively worse with LV concentric remodelling, eccentric LV hypertrophy, and concentric LV hypertrophy [5].

However, that classification depends on the ratio of wall thickness to LV dilatation and does not take the independent changes of LV wall thickness and diameter into account. Thus, Khouri et al proposed a new classification of LV hypertrophy into four groups, where both LV concentricity and volume were taken into consideration [6]. Their results suggested

that eccentric LV hypertrophy with no dilatation was associated with a lower risk for coronary artery disease and myocardial function impairment than the remaining three groups of cardiac hypertrophy. However, there were no results on outcome and the potential prognostic information from this proposed classification of LV hypertrophy remained unknown.

De Simone and colleagues [7] now report results in Journal of Hypertension on hypertensive LV geometric abnormalities as a risk factor for cardiovascular morbidity and mortality. They investigated 8848 treated hypertensive patients by echocardiography within an open registry in Southern Italy. Mean age was 53 years, 44 % were women, and obesity was present in 42 % and diabetes in 11 %. Incident cases of a composite outcome of non-fatal and fatal myocardial infarction, stroke and sudden death during a median follow-up of 35 months were recorded. Normal LV geometry was present in 66 %, concentric remodelling in 5 %, eccentric non-dilated in 20 %, eccentric dilated in 4 %, concentric non-dilated in 5 %, and concentric dilated LV hypertrophy in <1 %. Obesity was most common among patients with dilated LV hypertrophy forms, and almost one out of three with dilated concentric LV hypertrophy were diabetic. Compared to hypertensive patients with normal LV geometry, hazard ratios for a fatal or non-fatal cardiovascular event increased progressively from concentric LV remodelling through eccentric non-dilated, eccentric dilated, concentric non-dilated to concentric dilated (hazard ratios with 95 % confidence intervals): 1.20 [0.80–1.60], 1.23 [0.87–1.74], 1.95 [1.22–3.12], 2.16 [1.23–3.80], and 8.91 [2.17–36.59]. Of note, LV mass indexed for body size was the key parameter for future cardiovascular risk as LV mass and geometric pattern were associated.

These results by de Simone and associates [7] confirm and extend findings in a smaller group of 939 patients with hypertension-induced LV hypertrophy by ECG within the Losartan intervention for endpoint reduction (LIFE) study by Bang et al recently reported in Circulation: Cardiovascular

Imaging [8]. In this study normal LV mass was present in 21 %, concentric remodelling in 4 %, eccentric non-dilated in 12 %, eccentric dilated in 20 %, concentric non-dilated in 29 %, and concentric dilated LV hypertrophy in 14 %. Compared to normal LV geometry, the hazard ratio for all-cause mortality during a median follow-up of 59 months with eccentric non-dilated LV geometry was similar to patients with normal LV geometry, whereas eccentric dilated (2.7 [1.6–4.8]), and both concentric non-dilated (2.7 [1.6–6.6]) and dilated (3.2 [1.4–7.5]) LV geometry had an increased risk. Similar results were shown for cardiovascular mortality.

There are some potential limitations to the study by de Simone and associates [7]. The study is based on an open registry collecting data from general practitioners and community hospitals and maybe subject to selection bias. Concentric dilated LV hypertrophy was present in very few patients and conclusions about this geometric abnormality may be uncertain. Potential limitations to the study by Bang and colleagues [8] include the selection of patients by the presence of LV hypertrophy by ECG, and the low number of patients with LV concentric remodelling. Nevertheless, the relations between LV geometric pattern and predicted risk in both these studies appear to support earlier observations [6]. This suggests that the extent of both pressure overload and volume overload may be associated to the risk for future cardiovascular events. Further studies should examine whether these alterations in hemodynamic overload in hypertension should be addressed by tailored antihypertensive drug therapy in the individual patient to improve prognosis.

Hypertension is a major risk factor for heart failure. Diastolic dysfunction in hypertension and in heart failure with preserved LV ejection fraction is related to the extent of myocardial fibrosis, and myocardial fibrosis may precede the development of hypertension-induced LV hypertrophy [9–11]. Observations in heart failure patients with reduced LV ejection function suggest disturbances of collagen type I metabolism to be involved in cardiac remodelling, and augmented degradation of myocardial collagen scaffold may exacerbate heart failure by LV dilatation and impaired contractile function [12,13]. This may be related to cardiovascular mortality. It would be interesting to assess disturbances of collagen metabolism leading to alterations in myocardial collagen network in the context of the proposed new classification of hypertensive LV geometric abnormalities. Such information may help us to better understand the dynamic changes in myocardial extracellular matrix composition in relation to changes in LV geometry. This could improve our understanding of the transition from hypertension to heart failure, and may suggest new diagnostic and therapeutic directions.

In Conclusion

In conclusion, a new classification of hypertensive LV geometric abnormalities where LV mass and dilatation are given full consideration appears to improve risk stratification. The benefit of an improved risk assessment and appropriate treatment of hypertensive patients may be considerable.

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- Thomas Kahan

Hot off the Press



Dylan Burger

Ottawa, Canada

New Investigator and Communications Committee Member

AT2R Agonist, Compound 21, Is Reno-Protective Against Type 1 Diabetic Nephropathy

REFERENCES:

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Angiotensin II, the main effector of the renin-angiotensin system, has long been established as a central contributor to the progression of diabetic nephropathy. Indeed, Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II (Ang II) receptor blockers (ARBs) are well known to attenuate progressive glomerulosclerosis in disease models and can slow progression of diabetic kidney disease in humans. Mechanistically, Ang II binds to two G protein-coupled receptors known as the angiotensin II type 1 (AT1) and angiotensin II type 2 (AT2) receptors. AT1 is the best studied receptor and most of the classic effects attributed to Ang II (i.e., vasoconstriction, profibrotic, proinflammatory) are mediated by AT1 receptors. By contrast AT2 receptors appear to counteract AT1 receptor-mediated effects. However its role in health and disease is much less clear.

The above studies employed a selective nonpeptide agonist to the AT2R (Compound 21) in experimental mouse models of type 1 and type 2 diabetes. Koulis et al. employed a model of streptozotocin-induced diabetes in ApoE^{-/-} hyperlipidemic mice (type 1 diabetes) and found that Compound 21 administration over 20 weeks was associated with a significant reduction in albuminuria, and serum levels of cystatin c. as well as reduced mesangial expansion and glomerular collagen levels. These effects were accompanied by inhibition of renal oxidative stress and inflammation. By contrast, Compound 21 did not alter any of the analyzed parameters when administered to healthy mice.

Similarly, Castoldi et al. showed that Compound 21 attenuated renal injury in Zucker diabetic fatty rats (type 2 diabetes) as assessed by albuminuria, fibrosis, macrophage infiltration, and TNF- α expression. Interestingly, the administration of Compound 21 in combination with Losartan showed beneficial effects beyond what was seen by either treatment alone.

Taken together, these studies provide evidence that

Compound 21 may have benefit in diabetic nephropathy and that these effects may be expanded through combined administration with AT1R blockers.

- Dylan Burger

World Hypertension Day 17th May 2015



Read a special WHL-ISH Report: Celebrate World Hypertension Day (WHD) on May 17, 2015, and Contribute to Improving Awareness of Hypertension

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.

View www.worldhypertensionleague.org for further information.



[Watch this ISH video](#) -

Healthy BP
Tips from
ISHCast

Stéphane Laurent

Georges Pompidou European Hospital Hypertension Excellence Center

Paris, France

France is among the countries with the best results for management of hypertension in the population, as estimated by the proportion of hypertensive subjects whose hypertension is treated and controlled.

These results reflect, in part, the vitality of the French school of hypertension specialists in terms of both clinical practice and research in addition to the organization of the health care system in France with access to health care services and medications for all patients.

Aims of the Hypertension Excellence Center - HEC

- Prevention, diagnosis and treatment of hypertension and cardiovascular disease
- Optimization of models of clinical care for secondary hypertension
- Improvement of CV risk assessment and definition of best preventive strategies
- Discovery of novel therapeutic strategies for treating resistant hypertension
- Translation of mechanistic science into advances in clinical practice for rare and common arterial disease
- Translation of knowledge originating from HEC findings in basic and clinical research
- Establishment of national guidelines for the management of secondary hypertension
- Training and career development of young French and foreign doctors, both in research and clinical practice

History

In the 1970s, the pioneering work of Paul Milliez, together with Jean-Michel Alexandre, Pierre Corvol, Joël Ménard and

Michel Safar, was to organise and bring together all the facilities required for the management of difficult cases of hypertension at Broussais Hospital (hormone determinations, haemodynamics, pharmacology, physiology, etc...) and to initiate as early as the 1980's translational research using animal and cellular models with pioneering discoveries in the field of the renin angiotensin aldosterone system and the vascular hemodynamics. In 2000, Michel Azizi, Guillaume Bobrie, Gilles Chatellier, Xavier Jeunemaitre, Stéphane Laurent and Pierre-François Plouin transferred the hypertension unit into the newly built Georges Pompidou European Hospital (HEGP) in the 15th district in Paris and extended its clinical and research activities to clinical epidemiology, clinical investigation, clinical and pharmacological trials, and genetics. In 2006, the unit was labeled HCE by the European Society of Hypertension (ESH) (www.centre-hypertension.org) on the basis of medical and scientific quality and technological environment. Under the leadership of Pierre-François Plouin, the HCE brought together 22 physicians, including the physicians and researchers listed above, together with Laurence Amar, Pierre Boutouyrie, Anne-Paule Gimenez-Roqueplo and Maria Cristina Zennaro.

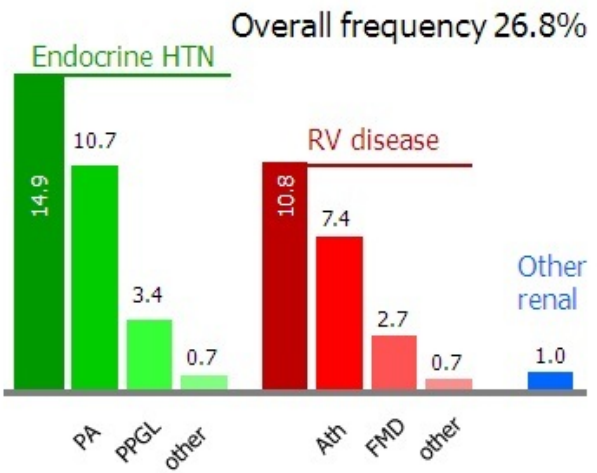


Clinical activity

The HEC is acknowledged by the French Ministry of Health as a reference clinical centre for rare adrenal diseases, including pheochromocytomas and Conn's adenomas, and for rare vascular diseases, including fibromuscular dysplasia. Overall,

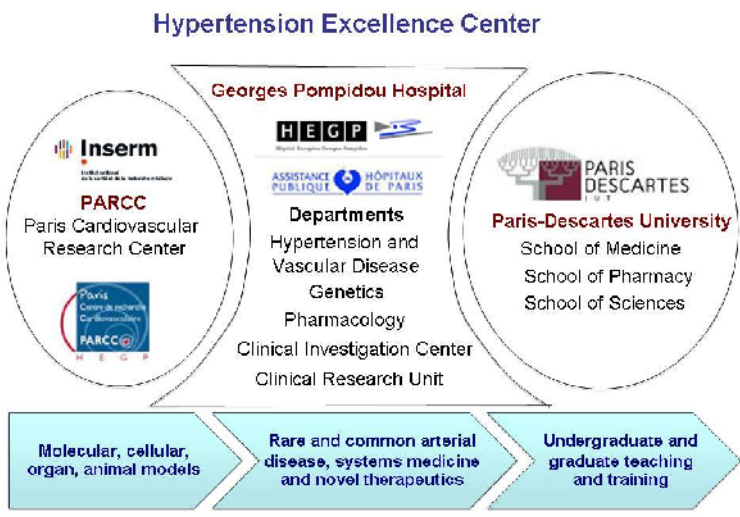
80% of the patients referred to our HEC have resistant or grade 3 hypertension, and 25% have secondary hypertension (these presentations are not mutually exclusive). Each year, the clinical activity combines more than 1500 hypertension-related hospitalizations, 4500 hypertension-related outpatient visits, and 450 hypertension-related procedures.

Percentages of patients with secondary hypertension (HTN) among those recruited by the HEC (Ath, atherosclerotic; FMD, fibromuscular dysplasia; PA, primary aldosteronism; PPGL, pheochromocytoma or paraganglioma; RV, renovascular):



Affiliations

The HEC encloses the departments of Hypertension (head, PF Plouin), Genetics (head, X Jeunemaitre), and Pharmacology (head, S Laurent), the Clinical Investigation Center (head, M Azizi), the two later being involved in pathophysiological and phase 1-3 pharmacological studies, and the Clinical Research Unit (head, G Chatellier) for large scale trials and clinical epidemiology. All are integrated in the "Common and rare vascular diseases" University Department and linked to the Paris Cardiovascular Research Center (PARCC) and Paris-Descartes University.



Georges-Pompidou European Hospital

HEGP is a 800 beds university hospital affiliated to Assistance-Publique Hôpitaux de Paris opened in July 2000. Important for hypertension care and research is the in-hospital access to:

- multi-disciplinary services, including Cardiology, Nephrology, Endocrinology, Angiology, Gynaecology, Ophthalmology, Neurology, Urology, Intensive Care, Surgery, Vascular Surgery, and Radiology departments.
- full imaging and laboratory facilities including Computed Tomography, Magnetic Resonance Imaging, total body Ultrasound imaging including high resolution Echo-tracking, Arterial Tonometry, ambulatory and teletransmitted home blood pressure monitoring, Isotopes including SPECT, PET-scan, and functional fusion imaging, Angiography (CT- and MR-angiography and digitized intra-arterial angiography); and Clinical chemistry, including Hormone and Pharmacology Laboratories and a Department of Genetics.

Paris Cardiovascular Research Center (PARCC) and hypertension-related research programs

Research at the HEC takes advantage of the close vicinity, within the same building, of the Paris-Cardiovascular Research Center (PARCC), the only center in France dedicated to basic science on vascular diseases. PARCC was funded in 2009 by the National Institute for Health and Medical Research (INSERM) and the Paris Descartes University. Among the 14 research teams of PARCC, 4 are mostly related to hypertension: "Pathophysiology, pharmacology and imaging of large arteries" (S Laurent) which focuses on imaging biomarkers, such as arterial stiffness; "Genetics of rare arterial disease" (X Jeunemaitre) with studies on fibromuscular dysplasia and Gordon's syndrome; "Pheochromocytoma and paragangliomas: from genetics to molecular targeted therapies" (AP Gimenez-Roqueplo); and "Genetic mechanisms of aldosterone-related disorders" (MC Zennaro) with studies on aldosterone-producing adenomas. Altogether, 23 senior scientists and associated clinicians, 13 PhD students, 14 post-doctoral and visiting fellows and technical assistants, and 9 master students participate to these research programs.

Research collaborations and teaching activities

The HEC coordinates multiple research programs which have given rise to hundreds of publications. It is the only French center involved in the development of international early (Phase 1-3) clinical trials for new drugs for treating hypertension (vasopeptidase inhibitors, renin inhibitors, aldosterone synthase inhibitors, and brain aminopeptidase A inhibitors). Members of the HEC are actively engaged in

teaching activities at Paris-Descartes University and foreign universities and in supervision of PhD students. They all deliver lectures at various international meetings. Each year, they organize a French inter-university Master Course in "Hypertension, a vascular and renal risk".

International and national learned societies

The HEC of HEGP coordinates the French network of HEC and conducts several multicenter clinical trials (DENER-HTN, SPARTE). Members of the HEC are active members of the French Society of Hypertension (SFHTA), ISH and ESH. PF Plouin, S Laurent and X Jeunemaitre have been Presidents of the SFHTA. S Laurent has been President of the ESH and ARTERY Society. X Jeunemaitre has been President of the European Conference on Cardiovascular Research (ECCR) and will be Chairman of the next ESH 2016 Meeting that will be held in Paris, France. PF Plouin is the President of the Endocrine WG of the ESH. M Azizi is member of the scientific council of the ESH. Pierre Boutouyrie is active member of ARTERY Society. MC Zennaro is President of the WG on aldosterone-secreting adenomas of ENS@T, member of the Executive Committee of the International Aldosterone Conference and President of ESAC France. AP Gimenez-Roqueplo is President of PRESSOR and the PHEO/PGL working group of ENS@T. All are involved in the organization of the Paris meeting of the ESH in 2016.

- Stéphane Laurent

**Prestigious
award to**

**Alta
Schutte,
South Africa**



Dear ISH Members,

It is my pleasure to inform you that Dr. Alta Schutte has been selected as one of the **Next Einstein Forum (NEF) Fellows in Africa**. The NEF Fellowship is a flagship program of the Einstein Forum (NEF). Alta is to be congratulated on having the kind of scientific record and potential for leadership that merits such an honour.

Lars H Lindholm, Editor

"Working together for better BP control and CVD reduction"
Hypertension Seoul 2016
The 26th Scientific Meeting of the International Society of Hypertension
September 24(Sat) - 29(Thu), 2016 COEX, Seoul, Korea
www.ish2016.org

**HAVE YOU PAID YOUR
2015 MEMBERSHIP FEE?
IF NOT - PLEASE**

Please note: Membership shall cease upon failure to pay the annual subscription fee for two consecutive years.

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ISH membership
for 2015 now



New Investigator Committee (NIC) Update



Dylan Burger

Ottawa, Canada / New Investigator and Communications Committee Member

Update from the Media Working Group of the ISH New Investigator Committee



The Media Working Group (MWG) works to promote activities of the ISH New Investigator Committee (NIC) with a focus on engagement through social media.

Media Working Group members

The committee consists of myself, Oneeb Mian, Ruan Kruger, Andre-Pascal Kengne, Ricardo Pena-Silva, as well as our newest members Lucinda Hilliard and Panos Xaplanteris.



Oneeb Mian



Ruan Kruger



Andre-Pascal Kengne



Ricardo Pena Silva



Lucinda Hilliard



Panos Xaplanteris

The following is a list of our major accomplishments from the past year:

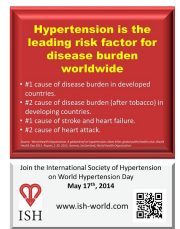
This past year was very successful for the MWG with our Facebook/Twitter presence expanding dramatically. This growth has been achieved through the efforts of everyone on the committee as well as ISH members who have supported our work since day 1. I would like to personally thank everyone who has contributed to the New Investigator initiatives for their support.



1. We debuted a **new logo** designed by Oneeb Mian.

2. We've added a **LinkedIn** profile thanks to Ruan Kruger. If you have not already done so please connect with us!

3. We produced a series of **educational posters** under the ISH brand for use on World Hypertension Day. These are available for members to distribute at their own institution for the coming year (and a gentle reminder that World Hypertension Day is May 17!)



3 different World Hypertension Day posters are available in English, Spanish and Portuguese.



4. We produced a host of **ISHCast Videos** including a new debut feature called ISHCast Editors Series where we interviewed Professors **Rhian Touyz** and **Anna**

Dominiczak for behind the scenes insight the workings of academic journals. These videos were very popular and we hope to follow up on those in the coming years.

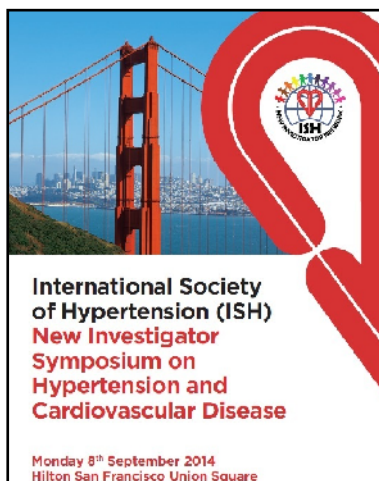
5. We helped organize and promote a fantastic **ISH Networking and Mentorship Event** in Athens.

Stephen Harrap and Junhua Zhou - Mentor & mentee



6. We provided **Twitter/Facebook** updates on 6 distinct scientific conferences

a. including two ISH-sponsored New Investigator Symposia in **Athens** and **San Francisco**.



All of these activities have really helped build the profile of the New Investigator Committee both within the ISH and in our international academic community as a whole.

As we look forward to the next year I am hoping to build on these initiatives. In addition we will be debuting a number of other new initiatives. One initiative which we are particularly excited about will be known as "What's on my desk" which would run monthly through our Facebook/Twitter accounts as well as the monthly updates. In this feature, senior scientists in hypertension / cardiovascular disease will be approached to provide the name /details for an article that they are interested in at the moment. This will provide our members with a unique opportunity to see articles which are of interest to field leaders in hypertension research.

- Dylan Burger

MEET THE ISH NEW INVESTIGATOR COMMITTEE (NIC) IN 2015

- **June:** European Society of Hypertension (ESH) Annual Meeting, Milan, Italy
An ISH NIC networking and mentorship evening event will take place on Saturday 13th June. Should you be interested in attending please email secretariat@ish-world.com.
- **August:** China Summer School
This event is being organised in conjunction with the ISH Asia and Australasia Regional Advisory Group (RAG) and will be attended by NIC members - Sofie Brouwers and Fadi Charchar.
- **Sept:** Council on Hypertension of the American Heart Association (AHA) Scientific Sessions
The NIC will hold joint Oral and Poster Presentation Award sessions with the Trainee Advocacy Committee of the Council on Hypertension and contribute to their mixer event. Abstracts should be submitted via the AHA submission site.

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IMPROVE-IT – combination therapy comes of age



Colin Baigent

Professor of Epidemiology, Clinical Trial Service Unit & Epidemiological Studies Unit (CTSU), University of Oxford, UK

IMPROVE-IT – combination therapy comes of age

For the treatment of low density lipoprotein (LDL) cholesterol, the concept that 'lower is better' is supported by two main types of evidence. First, in observational studies there is a positive log-linear relationship between cholesterol and coronary heart disease risk throughout the range of cholesterol studied. Secondly, randomized trials have shown that, as compared to standard statin regimens, additional reductions in LDL cholesterol with more intensive statin regimens further reduce the risk of major vascular events. As is predicted by the absence of any inflection at low cholesterol concentrations in observational studies, further reduction of LDL cholesterol yields additional benefit even among those with low LDL cholesterol. The Cholesterol Treatment Trialists' (CTT) meta-analysis of 5 large trials comparing more vs less intensive statin regimens showed that further reduction in LDL cholesterol was beneficial even among those with LDL cholesterol less than 2 mmol/L (80mg/dL) – in whom allocation to more intensive statin treatment reduced LDL cholesterol on average from about 1.7 mmol/L to about 1.3 mmol/L.

The consistency of the observational and randomized trial evidence implies that the mechanism through which statin therapy reduces risk is by lowering LDL cholesterol. This, in turn, suggests that drugs which reduce LDL cholesterol when added to a statin might also be effective in reducing risk. The IMPROVE-IT trial addressed this hypothesis by assessing the ability of ezetimibe to add to the benefits of statin therapy. Ezetimibe reduces cholesterol absorption by inhibiting the Niemann-Pick C1-like protein in the brush border of the gut, and it achieves about a 20% further reduction in plasma LDL cholesterol when added to a statin. In IMPROVE-IT, a total of 18,144 patients aged 50 or over and within 10 days of admission for an acute coronary syndrome were randomized to simvastatin 40mg plus ezetimibe 10 mg daily versus simvastatin 40mg daily alone. The primary composite endpoint was cardiovascular death, myocardial infarction, documented unstable angina requiring re-hospitalization, coronary revascularization, or stroke. The addition of ezetimibe was reported to yield a further reduction of 16.7 mg/dL (0.4 mmol/L) in LDL cholesterol as compared to simvastatin alone at 1 year, and this translated into a significant ($p = 0.016$) 6%

reduction in the risk of the primary endpoint (hazard ratio 0.936, 95% confidence interval 0.887-0.988), with an absolute benefit at 7 years of 2.0% (32.7% vs 34.7%). Benefit was achieved without any significant excesses of cancer, muscle or gallbladder-related events. The investigators have demonstrated, in post-hoc analyses that took account of missing laboratory data on LDL cholesterol, that the reduction in risk of major vascular events achieved by ezetimibe in the IMPROVE-IT trial was nearly identical to that resulting from the same absolute LDL cholesterol reduction by a statin in the CTT meta-analysis.

The IMPROVE-IT trial shows that ezetimibe can be used as a means of reducing atherosclerotic risk further among high-risk patients treated with simvastatin, but it is reasonable to extrapolate this to the use of ezetimibe when added to other statin regimens. The addition of ezetimibe to a statin regimen yields approximately the same additional reduction in LDL cholesterol as can be achieved by an 8-fold increase in the statin dose (since each doubling yields about a 6% additional reduction in LDL cholesterol), and we now know that the risk reductions in major vascular events from each strategy are similar. Patients who might benefit from adding ezetimibe to a statin therefore include those who remain at high risk despite maximum intensity statin therapy (since the statin dose cannot be increased). Another group of high-risk patients for whom combination therapy will be useful is those in whom high-dose statin therapy is associated with safety concerns, such as patients with chronic kidney disease where there is a risk of raised plasma statin concentration due to reduced renal clearance. Indeed, this was the rationale for using the combination of moderate-dose statin therapy (with simvastatin 20mg daily) plus ezetimibe in the Study of Heart and Renal Protection (SHARP) that previously demonstrated that this combination is indeed effective at reducing atherosclerotic risk in patients with chronic kidney disease. The use of ezetimibe alone might also be an option in patients who cannot tolerate statin therapy at all, but – as has been shown by the demonstration that atorvastatin 20mg could be tolerated by 75% of so-called 'statin-intolerant' patients in the blinded ODYSSEY-ALTERNATIVE trial presented at the

American Heart Association sessions in 2014 – such patients may be less frequent than is widely believed.

IMPROVE-IT provides strong support for the principle of combining different lipid-modifying treatments to achieve and sustain the lowest possible LDL cholesterol in high-risk patients. This is particularly relevant now because several proprotein convertase subtilisin/kexin (PCSK)-9 inhibitors in development can reduce LDL cholesterol by 60-70% when given on top of statin therapy. If ongoing trials establish both the efficacy of PCSK-9 inhibitors for reducing risk and their safety (in particular, when maintaining LDL cholesterol levels at very low levels), then there is the prospect of achieving very large benefits by combining LDL-lowering drugs. For example, combining a high-dose statin, ezetimibe and a PCSK9 inhibitor could

result in treatment regimens that reduce LDL cholesterol by 80% or more. If PCSK-9 inhibitors are as effective at reducing risk as is predicted by the CTT meta-analysis, then long-term use of such a combination regimen in a patient with a plasma LDL cholesterol concentration of, say, 4 mmol/L would be expected to yield a two-thirds reduction in the risk of major vascular events.

The key achievement of IMPROVE-IT, therefore, has been its validation of the strategy of combining a statin and a non-statin LDL-lowering drug to achieve further reductions in risk, and it seems likely that strategy will now be refined by future trials seeking to achieve even larger reductions in risk among high-risk patients.

- Colin Baigent

Council's Corner: Hypertension Issues - a personal view



Naftali Stern

Institute of Endocrinology, Metabolism and Hypertension, Tel Aviv-Sourasky Medical Ctr; and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Cognitive Protection in Hypertension: Ready for Prime Time

Over the past 65 years, the field of hypertension embodied a glorious journey from the "rice diet" and a handful of hardly tolerable drugs with limited effects on blood pressure all the way into a diversified supermarket of highly effective anti-hypertensive armamentarium.

Malignant hypertension, a frequent killer in the fifties has nearly vanished and fatal- as well as non- fatal hypertension-related events have decreased dramatically enough to make it hard for contemporary clinical trials to discern, in terms of event rate, between alternative protocols of anti-hypertensive treatment or between the benefits attained by one level of achieved on-treatment blood pressure and an even better controlled hypertension. These major changes have been accompanied by a creeping alteration in the "average" hypertensive phenotype: often abdominally obese, sedentary and/or diabetic; less inclined to smoke, perhaps, but an avid consumer of salty and processed food, and last, but not least, older: no less than 15 years of life have been added within this time frame to the average lifespan, much of it owing to better blood pressure and lipid control.

As the phenotype of our hypertensive patients changes, the "gold standard" tools to assess the impact of treating of hypertension that have thus far dominated the field are, in my opinion, ripe for reconsideration. This would reflect no shred of disrespect for the ongoing quest to reduce

heart disease, stroke and renal failure, but rather, a simple appreciation of the growing problem of cognitive loss within the recently gained, last 15 years of life. In all published analyses, hypertension is an important player in dementia. Better cognitive protection, not through stroke prevention alone, seems mandatory if one is to bring more life into the already added years of life. It is critical to understand how hypertension, obesity, insulin resistance, diabetes, aging and genetic background, separately and in combination, affect the brain. Wonderful tools are now available to visualize brain structure and function, assess cerebral blood flow and test cognitive performance. Circulating surrogate markers of brain health are under development. The study of brain in hypertension has lagged far behind the insights gained in the cardiorenal/vascular arena. This must change. To protect the brain from increased blood pressure, we need new means and better understanding. But, at the very least, we simply need to know how the tools we are already using in hypertension affect the brain: which drug class, what blood pressure level at which cost in cerebral flow might possibly yield better cognitive outcome? To phrase it bluntly: more research funding must be diverted to the "hypertensive brain"; and no future clinical trial in hypertension should be conducted without a genuine attempt to offer at least some cognitive endpoints.

- Naftali Stern

Council's Corner: Hypertension Issues - a personal view

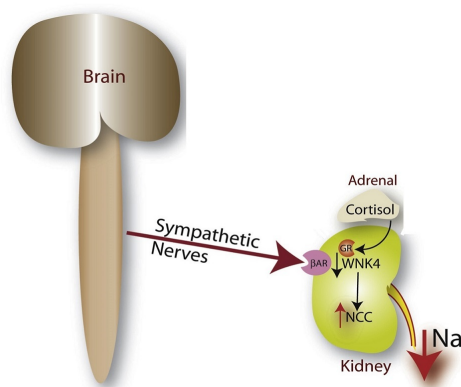


Richard Wainford

Dept. of Pharmacology & Experimental Therapeutics and the Whitaker Cardiovascular Institute, Boston, USA

Salt-sensitive hypertension –what does the future hold?

Hypertension represent a global health epidemic that is predicted to affect over 1.5 billion individuals by the year 2025 and salt-sensitive hypertension is a significant component of hypertension. Salt-sensitivity affects approximately 50% of hypertensive patients, leading to a 3-fold increase in the risk of adverse cardiovascular events compared to salt-resistant hypertensive patients. It is well established that integrated neural, humoral, and renal mechanisms are implicated in the pathogenesis of salt-sensitive hypertension. Interest in enhancing our understanding of the neural mechanisms involved in hypertension, and salt-sensitivity in particular, has been renewed by 1) the elegant work of Dr. Fujita who demonstrated a direct role of renal sympathetic innervation in the dysregulation of the renal sodium chloride co-transporter as a key event in the pathophysiology of salt-sensitive hypertension (1) and 2) the conflicting results of the SYMPPLICITY HTN trials in which renal nerve ablation produced both persistent blood pressure reduction (HTN 1 & 2) and a lack of effect versus placebo (HTN-3). Despite decades of pioneering work enhancing our knowledge of the neural control of the kidney (2) and recent insights into the regulation of renal sodium transporters, as illustrated schematically, the central mechanisms regulating sympathetic nerve traffic to the kidney remain to be defined.



(Adapted from Ellison and Brooks, 2011 Cell)

Here in Boston, in the Department of Pharmacology & Experimental Therapeutics and the Whitaker Cardiovascular Institute, we have been investigating the integrated neural

control of blood pressure, with a particular focus on the central regulation of the renal sympathetic nerves. These investigations have revealed the presence of an endogenous central molecular signal transduction pathway, Gai2 subunit proteins (which facilitate signal transduction following GPCR activation), that is required to mediate the acute renal sympathoinhibitory, hypotensive, and natriuretic responses to both pharmacological and physiological stimuli. Significantly, endogenous up-regulation of hypothalamic PVN Gai2 proteins in salt-resistant animal models in response to increased salt-intake is required to potentiate endogenous renal nerve dependent sympathoinhibitory sodium excreting mechanisms to counter the development of salt-sensitive hypertension (4). We postulate that this central molecular pathway compliments the ground breaking research of the Fujita lab and provides a potential mechanism in the central nervous system through which renal nerve activity is regulated to influence renal regulation of the sodium chloride co-transporter in both salt-resistant and salt-sensitive rat phenotypes.

Owing to the increasing worldwide prevalence of hypertension, and the role of dietary salt-intake in the pathophysiology of this disease (5), it is clear that increased understanding of the central mechanisms involved in blood pressure regulation, in both normotensive and salt-sensitive hypertensive animal models and humans is required. A significant number of key questions pose barriers to our understanding of the pathophysiology of salt-sensitivity including; how and where is salt-sensed by the body? What mechanistic responses are activated to maintain salt-resistance and do these represent future therapeutic targets? How can you rapidly and reproducibly assess salt-sensitivity in human patient populations? Can non-invasive biomarkers of salt-sensitivity be identified? I look forward to the answers to these issues being addressed by the global hypertension community in the coming decades to enhance to our ability to understand and combat the global hypertension epidemic.

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- Richard Wainford

Gender aspects in hypertension treatment



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Gender aspects in hypertension treatment

Introduction

Hypertension is the most important modifiable cardiovascular risk factor in both women and men. Blood pressure >115/75mm Hg is strongly and directly related to vascular and overall mortality in both gender in middle and older age 1. For hypertensive patients, the decrease in total life expectancy is 5.1 years in men and 4.9 years in women compared to normotensive subjects 2. Hypertension is more common in younger males but the prevalence in women is increasing with age, thus in the population hypertension is equally common in women as in men 3.

Blood pressure levels differ between women and men in different ages. Young men have a higher blood pressure, both systolic and diastolic blood pressure, compared to young women. Systolic blood pressure steadily increases with advancing age in both sexes. Diastolic blood pressure rises until the fifth decade and then decreases in both women and men. Since the age-related rise in systolic blood pressure is more pronounced in women, pulse pressure is higher in women post menopause compared to age matched men 4.

The differences between women and men regarding blood pressure levels are consistent in different populations and are also found in animals⁵. The fact that younger men have higher blood pressure and that blood pressure in women begins to rise after the fifth decade of life have suggested that gonadal hormones and/or sex chromosomes complement can be involved in the development of hypertension. However the connection is complex.

Several investigations have shown that menopause is associated with an increase in blood pressure also after adjustments for age and body mass index 6. 17 β -Estradiol (E2) prevents blood pressure from rising after ovariectomy in several different mice models, supporting the conclusion that loss of oestrogen may increase blood pressure 7. At menopause E2 levels drop, but several other changes occur that cannot be separated from the decline in E2. Testosterone declines and FSH and LH increase just after menopause. Accordingly, hypertensive men have lower testosterone levels

compared to normotensive men. Treatment for testis cancer where testes are removed results in a higher blood pressure, suggesting that testosterone may also play a role in the regulation of blood pressure 8. Furthermore, testosterone is converted to E2, hence lower testosterone levels results in lower E2 levels. However, women with polycystic ovarian syndrome have higher testosterone levels and also higher blood pressure compared to healthy women.

Salt sensitivity correlates inversely with circulating ovarian hormones 9. It has been suggested that salt sensitivity after menopause contribute to a higher blood pressure in postmenopausal women 10. Furthermore, it has been implied that oestrogen might influence blood pressure in women through stimulation of nitric oxide and that the salt sensitivity in postmenopausal women is related to abnormal vascular reactivity, which is mediated through nitric oxide 11.

On treatment blood pressure control

In patients with hypertension there are contradictory results regarding gender and blood pressure control from observational and cross-sectional studies. Women are in some studies more likely to be treated but less likely to achieve blood pressure control 12, 13. A recent publication shows that women treated in primary health care in Sweden are less likely to achieve blood pressure control¹⁴. However, in other investigations women are more likely than, or just as likely as men, to achieve blood pressure control. There seems to be an age-dependent relationship between blood pressure control and gender, where younger men and older women have lower rates of blood pressure control 15. Blood pressure levels in hypertensive patients follow the same pattern as in normotensive subjects in most parts of the world, as illustrated in figure 1. Furthermore, there is evidence to suggest that the gender of the physician and the patient may influence the ability to reach target blood pressure 16.

Antihypertensive treatment

In early randomized trials regarding hypertension women were not included. Over the years women have been included

to an increasing extent; however, the lower absolute cardiovascular risk in women made the benefit of antihypertensive therapy on cardiovascular outcome more difficult to prove. This resulted in a discussion regarding the therapeutic benefit in treatment of women with moderately elevated blood pressure. Several reviews have concluded that gender differences in response to antihypertensive therapy have not been investigated completely and emphasize the need for more data to guide the management of women with hypertension 17.

The evidence for the benefit of antihypertensive treatment in both women and men has increased. A large analysis could conclude that there was no evidence of a gender difference in response to different antihypertensive drugs in randomized controlled trials. However there was borderline significant evidence ($p=0.05$) that women derived greater protection from stroke with regimens based on calcium channel blockers, compared to regimens based on ACE inhibitors 18. Nevertheless, it supports current guidelines, which state that there should be no special considerations regarding antihypertensive drug class based on the patient's sex. The only exception is in pregnant women, where ACE inhibitors and ARB should be avoided due to teratogenic effects. In patients with diabetes mellitus and chronic kidney disease antihypertensive treatment with ACE inhibitors or ARB is recommended.

Despite guidelines, observational trials in both Europe and the United States have shown that women and men are treated with different antihypertensive drugs 12, 13. In general, women are more often treated with diuretics or beta adrenoceptor blockers and men with ACE inhibitors or calcium channel blockers¹²⁻¹⁴. We recently found the same pattern in prescription pattern in primary health care in Sweden, but the reasons for this are not clear¹⁴. The gender differences in antihypertensive treatment in patients with concomitant cardiovascular disease seem to be smaller. Thus, presence of comorbidities could maybe explain the gender differences in prescriptions. However, this explanation could not be confirmed in our investigation¹⁴. Another possible explanation could be gender differences in side effects. Women more often react with cough when treated with ACE inhibitors compared to men. However, women could then be treated with an ARB instead according to guidelines, but this replacement was not found in our recent investigation¹⁴. Neither did we find that ethnicity, educational level or signs of psychiatric discomfort could explain the gender differences in antihypertensive prescriptions¹⁹. Women do seem to be more susceptible to vasodilation-related adverse symptoms by dihydropyridine calcium channel blockers, which could contribute to a lower prescription rate of calcium channel blocker to women 20. The clinically

noticed problem of swelling amongst older women has also been suggested as an explanation to the higher prescription rate of thiazide diuretic to women. But to conclude, there is up to now no robust explanation to the gender differences in prescription pattern of antihypertensive drugs.

End organ damage cardiovascular disease and drug therapy

Even if the choice of antihypertensive treatment always should be based on the individual character of the patient some important gender aspects should be considered. Thiazide diuretics and beta adrenoceptor blockers have known negative metabolic effects, which are enhanced if the two drugs are combined, and they may induce diabetes mellitus. Women with diabetes have been shown to have a higher risk of cardiovascular morbidity and mortality compared to their male counterparts 21. Since women get more disabled following a stroke compared to men²², and beta adrenoceptor blockers have an inferior capacity on reducing stroke risk compared to other antihypertensive drugs, the current treatment tradition with prescription of thiazide diuretics and beta blocker to women could be questioned.

According to guidelines patients with hypertension and diabetes mellitus are recommended treatment with ACE inhibitors or ARB, especially in the presence of proteinuria and microalbuminuria, and ACE inhibitors or ARB are regarded as first line antihypertensive treatment in patients < 55 years. These recommendations emphasize the risk evaluation in patients with a low 10-year risk but a high life time risk of cardiovascular disease, which is common in younger patients and in women.

Women with atrial fibrillation have an increased risk of stroke compared to men and women who suffer from stroke more often have atrial fibrillation and hypertension as risk factors compared to men 23. In this context it is interesting to notice that ACE inhibitors and ARB also may reduce the risk of new onset atrial fibrillation among hypertensive patients. We know that left ventricular hypertrophy (LVH) is an independent risk factor for cardiovascular disease in both women and men and LVH is present in approximately 30% of patients with hypertension. There is however evidence that LVH is a stronger risk factor in women than in men 24. In light of this it seems appropriate to offer women with hypertension treatment with drugs blocking the renin-angiotensin system.

Hypertensive conditions exclusively found in women

The use of combined oral contraceptives is known to increase blood pressure, sometimes with as much as five mm Hg²⁵. Blood pressure levels return to normal values after cessation of therapy, but in some cases blood pressure may be elevated for months past treatment 26. In a recent

investigation no association between duration of hormonal contraception and later hypertension was found in postmenopausal women 27.

Five to 10 percent of all pregnancies are complicated by a hypertensive manifestation. Most women experiences a hypertensive pregnancy without major complications, but still hypertensive pregnancies remain a threat both to the woman and the foetus and are a major cause of maternal mortality worldwide²⁸. Besides being hazardous during pregnancy and the puerperium several epidemiological studies after hypertensive pregnancies have presented solid evidence of an increased maternal cardiovascular risk later in life²⁹⁻³¹.

The pathophysiological mechanisms behind preeclampsia and gestational hypertension differ, where gestational hypertension may be looked upon as a disposition for hypertension, which is "revealed" when the cardiovascular system is encumbered during the pregnancy. The pathophysiological changes behind preeclampsia however, seem to start early after conception and include activation of the immune system. An important mechanism behind the subsequent rise in blood pressure levels is a damaged endothelium 32, 33.

Pharmacologic treatment of high blood pressure during pregnancy can be initiated after preposition of the mother and the foetus. All kinds of blockade of the renin-angiotensin system should be avoided during pregnancy, but not during lactation. Beta adrenoceptor blockade, treatment with calcium channel blocker and hydralazine are drugs frequently used during pregnancy, and chronic hypertension demand a somewhat different approach to treatment compared to the diagnose preeclampsia (<https://www.nice.org.uk/guidance>)

In summary

Hypertension is an important cardiovascular risk factor in both men and women, and the prevalence is similar in both genders even though systolic blood pressure levels increase more beyond middle age in women, probably related to hormonal changes associated with the menopause. Several investigations demonstrate that blood pressure control is worse in women despite results from randomized controlled trial where the benefit of treatment is convincing in both genders. Women and men are prescribed different drug classes with predominance for beta adrenoceptor blockers and thiazide diuretics in women and ACE inhibitors and calcium channel blocker in men. The rational for this discrepancy is not completely understood, but variation in side effects or different evaluation of total cardiovascular risk in women and men might partly explain the finding. Combined oral contraceptives increase blood pressure in all women, even if established hypertension is uncommon and cessation of treatment always result in return of blood

pressure to pretreatment levels. Blood pressure increase during pregnancy could be a result of chronic hypertension or related to preeclampsia. In both situations specific knowledge of the caregiver is desirable since this hypertensive state demand specific antihypertensive treatment.

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- Charlotta Ljungman and Karin Manhem

COMMENTARY

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Doctors Ljungman and Manhem provide an interesting review of several aspects of hypertension management in relation to gender and bring focus to the fact of how little we know in the area.

The differential BP levels and hypertension rates by gender which they describe also differ with degrees of socio-economic development and age distribution of populations which will also impact on treatment and control rates.

The general observation that women often appear more likely to be treated for hypertension, may in part at least be due to an ascertainment bias, driven by regular BP-screening before or during oral contraceptive use and pregnancy. However reduced control rates among treated women compared with men have a less obvious explanation.

We are increasingly advised to base cardiovascular (CV) intervention – (be it lipid – or BP-lowering therapy) on the basis of estimated CV risk. However, the upshot of such an approach in practice would invariably mean that for any standard set of CV risk factors – women would be treated less than men. Nevertheless, perhaps for politically-correct reasons, differential treatment thresholds or targets are not recommended for men and women in any current hypertension guidelines.

Despite that, one wonders if less aggressive treatment is supplied to women on the basis of the physician's knowledge that women are at reduced average absolute CV risk compared with men.

The different agents reportedly used to treat women is also interesting. The particularly adverse effects of diuretics and beta-blockers on sexual function in men would seem a possible likely explanation for less use among men, whereas sexual dysfunction in women on antihypertensives is less clearly established.

Meanwhile, although not a consistent finding in trials, it

would be wrong not to mention the differential effects of ACE-inhibition versus diuretics in the ANBP2 trial which suggested that ACE-inhibitors were only superior at preventing CV events in men and not women!

The authors mention the interesting fact that the (relative) risk of CV events associated with diabetes appears to be greater among women than men, but more importantly – women with diabetes of several years duration assume the same absolute risk of CV events as diabetic men – wiping out the relatively lower rates of CV disease which women enjoy otherwise. Perhaps there are lessons there about what really protects women from CV disease?

Perhaps there are lessons there about what really protects women from CV disease?

- Neil Poulter

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~~ In Memoriam ~~



We regret to inform you that Dr. John H. Laragh, MD, ISH President (1986-1988) and the Founding President of the American Society of Hypertension, Inc. (ASH) passed away on Friday, 20th March 2015.

The ISH leadership would like to send their heartfelt sympathy to Dr. Laragh's family, friends and colleagues.

Dr. John H. Laragh

18 November 1924 - 20 March 2015

ISH President 1986-1988

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

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ISH Secretariat Contact Details

The ISH Secretariat moved from Hampton Medical Conferences to The Conference Collective on 1st April 2014.

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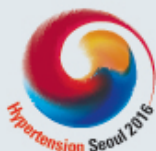
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***"Working together for better
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Notification of Acceptance	April 25, 2016
Opening of Online Registration	September 24, 2015
Early Bird Registration Deadline	May 16, 2016
Pre-Registration Deadline	July 31, 2016



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