HYPERTENSION NEWS

June 2014, Opus 37

We hope to see you at the Hypertension Athens (Joint ESH-ISH) meeting this week!

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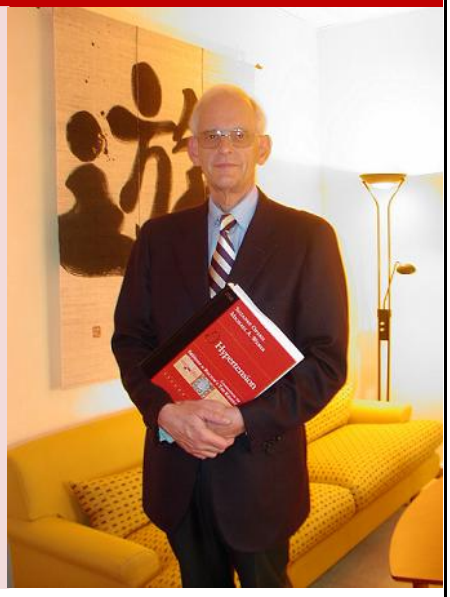
NOTES FROM THE EDITOR

Lars H. Lindholm

Dear ISH Member – Athens here we come!

It is my pleasure to present Hypertension News Opus 37 to you, in advance of the ESH/ISH meeting in Athens.



In this issue, you will find two new headlines.

***First*, "Hot off the Press – Basic Science"** written by Dr. Dylan Burger, Canada. Dylan Burger will broaden the "HOT off the Press" section, previously dominated by reports on clinical and/or epidemiological papers and written by Dr. Bo Carlberg, Sweden and/or by me.

***Second*, "The Council's Corner"** where some of our Council members have been asked to express their views on hypertension issues. First to contribute are Dr. Aletta Schutte, South Africa and Dr. Michael Weber, USA. Two or three papers from different members will follow in future issues of HT News.

In our previous issue (Opus 36), we published three papers on "Renal denervation". Shortly after our publication, Ms. Wendy Dougherty, US, Director of Corporate Communications at Medtronic, asked us to publish "corrections" of the papers written by Dr. George Bakris, US and Dr. Peter Sever, UK. You will find her comments on page 12. George Bakris waived responding. Peter Sever has sent us a fairly comprehensive response entitled "Who's kidding whom or, in search of the truth", which you will find on pages 13-14.

"What did HYVET really tell us" wonders Dr. Bo Carlberg, referring to a paper, recently published in Journal of Hypertension and an Editorial Commentary published in the same issue. Bo Carlberg's main point is that two thirds of the data in HYVET comes from the study of old patients who were taken off blood pressure lowering treatment before the start of the trial. In The Swedish Trial in Old Patients with Hypertension (STOP), the corresponding figure was about 50%. Hence, it seems clear that we should refrain from stopping blood pressure lowering treatment in the very old unless there is a strong indication for doing so. One wonders: Is that what current guidelines advise us to do?

In this issue you will find an interesting description of the "South African Scenario" compiled by Brian Rayner and Lionel Opie.

Below you will also find a farewell from Dr. Ernesto Schiffrin, Canada who steps down as President of the ISH in Athens and is succeeded by Dr. Rhian Touyz, UK. The members of the Communication Committee thank Ernesto Schiffrin for an excellent collaboration and a job well done.

Have a good read!

Lars H Lindholm, Editor

FROM THE ISH PRESIDENT, A FINAL REPORT

Ernesto Schiffrin, MD, PhD

Dear members of the International Society of Hypertension,

At the end of my mandate as President I wish to recapitulate for you briefly some of the salient moments of my period as President of ISH.

I started my Presidency at a very auspicious time, the scientific meeting of ISH in Sydney, Australia, in October 2012. My first objective at the time was to organise a retreat of the leadership and prominent senior and younger members of the society to re-examine our direction and decide on activities that would enhance the profile and functioning of ISH at the same time that they contributed to increase awareness of hypertension and improve the management of high blood pressure around the world. Accordingly we met in Milan in June 2013, an intense meeting that came up with a number of recommendations that are in the course of being implemented, and which I have referred to in detail in a previous report published in this Newsletter last year.

A pet project of mine that I defended vigorously during the retreat was revisiting the Guidelines for management of hypertension from ISH, last issued in 1999 together with WHO, and updated in a statement in 2003. I felt that we needed a simple document that would provide evidence-based guidance where evidence was available, and expert opinion when there was no evidence, a user-friendly document that would be easily accessible to physicians, particularly in low and middle-income countries. I thought that such a short and easy to follow document could contribute to improve control of blood pressure, and thus reduce heart attacks, strokes, heart failure, etc., particularly in resource-poor healthcare systems where hypertension is increasingly prevalent, and where guidance with the use of any antihypertensive available and goals to be reached could be beneficial to the increasing population of hypertensive patients. As the project evolved, we partnered with the American Society of Hypertension and after prolonged discussion came up with what is now referred often in the literature as the ASH-ISH Guideline, published simultaneously in J of Hypertension and in J Clin Hypertension online before print on December 17, 2013, and in print in January 2014. The Guideline has been better received than other guidelines published around the time because of its simplicity and its concern for evidence where there it exists, and for supporting valuable and proven interventions in relation to resources available in differing healthcare systems.

Another activity that I have encouraged is partnering with the World Hypertension League (WHL), a sister society more involved in public policy and prevention in the field of hypertension. We were able to jointly produce a statement published in February 2014 on salt reduction and its benefits for blood pressure control and reduction of morbidity associated with different forms of cardiovascular disease. We also associated with WHL in producing a Hypertension Fact Sheet that summarises some critical aspects of hypertension in a very readable format. We look forward to further successful collaborative activities jointly with WHL.

We are now heading rapidly toward the Athens meeting. We are looking forward to a great meeting of intense scientific exchange, as well as renewal of old friendships and opportunities for development of collaborations between scientists, clinicians and individuals involved in public health activities.

The Regional Advisory Groups (RAGs) represent different areas of the world, and have allowed us to identify meetings where ISH representatives have been present to speak and disseminate knowledge about hypertension. The African seminars organised by Professor Robert Fagard have been reported previously in the Newsletter. In Latin America, South East Asia, China, the Middle East, different activities have taken place, most already reported in detail in previous editions of this Newsletter, supported by ISH with one or two speakers and the cost of their travel, contributing thus to knowledge translation and implementation of guidelines for management of hypertension, hopefully leading to greater control of blood pressure.

An important aspect of ISH has been the activity of the New Investigator Committee, successfully led by a group of very enterprising young scientists, who have shamed us with their unending enthusiasm, dynamism and energy, which we in the Executive could hardly keep up with. Our Communication Committee has been extraordinarily active, as you can verify from the exceedingly successful production of this Newsletter, and we owe a big debt of gratitude to the endless energy and passion of Lars Lindholm, who has steered the Newsletter to new heights with every issue.

Among the activities that took a lot of our time was the transfer of service provider from Hampton Medical Conferences to the Conference Collective, in order to improve the service that we were providing our members as well as for functional efficiency in some of the actions of the organisation. The transfer was onerous and required legal advice, but has resulted in a leaner management of our Society. In this transfer we have been fortunate to retain Mrs. Helen Horsfield in the management of our Secretariat, which Helen has performed with extraordinary dedication and extreme efficacy for many years.

A concern that we in the Executive have had over the last few years has been to ensure that ISH continues to be well-funded and able to carry out its many activities, including that of the Regional Advisory Groups (RAGs), communications, support for the NIC Symposium, travel grants, etc. This was a matter of intense discussion at our retreat, in view of the mergers that occur in Industry, and the evolution of patents that decides the effort that Industry makes to support academic and research activities related to their products. Our Vice-President, Professor Louise Burrell, has been in charge of engaging with Industry to ensure that corporate affiliation was extended into the future. At the same time, we have been lucky to receive the contribution from the Vancouver ISH meeting, for which we are very grateful to the great effort performed by Dr. Simon Rabkin and his team, and from the Sydney meeting, for which we are very grateful to Dr. Gary Jennings and his team. This income will allow ISH to continue many of its ambitious programmes in the future.

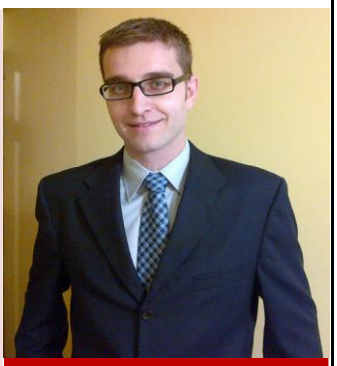
It has been a privilege and an honour to be President of ISH, which has given me the opportunity to be in contact and interact with many extremely fine individuals in the Executive of ISH and its Council, as well as its membership. I now leave the Presidency of ISH in the very able hands of Prof. Rhian Touyz of Glasgow University, and am sure that ISH will continue in its increasingly successful trajectory. Again, thank you all for your trust and friendship.

Ernesto L. Schiffrin
President, ISH (2012-2014)

Hot off the Press

Basic Science

Cardiac fibroblast-derived microRNA passenger strand-enriched exosomes mediate cardiomyocyte hypertrophy.



Dylan Burger
Communications & NIC Member

Bang C, Batkai S, Dangwal S, Gupta SK, Foinquinos A, Holzmann A, Just A, Remke J, Zimmer K, Zeug A, Ponimaskin E, Schmiedl A, Yin X, Mayr M, Halder R, Fischer A, Engelhardt S, Wei Y, Schober A, Fiedler J, Thum T.

J Clin Invest. 2014 May 1;124(5):2136-46.

Soluble factors such as small molecules and peptides have long received the bulk of experimental attention related to intercellular communication and (not surprisingly) constitute the large majority of drugs. Nevertheless, a growing body of evidence suggests that many biological processes may be influenced or even mediated by small extracellular vesicles released from cells. One such process may be ventricular hypertrophy. Hypertrophy in response to pressure overload involves physiological alterations to both cardiomyocytes and interstitial fibroblasts however cross-talk between these two cell systems is not well understood.

In the above study, Bang and colleagues [1] identify a novel intercellular signalling pathway between cardiac fibroblasts and cardiomyocytes involving exosomes: small (40-100 nm) phospholipid vesicles of endocytic origin. In an elegant series of experiments involving both cells and whole animal experiments, the authors illustrate how exosomes, formed from cardiac fibroblasts, transfer microRNA (miR) from fibroblasts to cardiomyocytes. This paracrine signaling event resulted in functional transfer of the miR (miR-21*) and an increase in cardiomyocyte size. Consistent with this response, the authors identify several gene targets that are altered by miR-21* in cardiomyocytea including several proteins involved in cytoskeletal regulation (i.e. Desmin, filamin-A, and myosin-6). Further support for a pro-hypertrophic effect of miR-21* was shown in a mouse model of angiotensin II-induced hypertrophy where inhibition of miR-21* reduced the hypertrophic response.

Taken together the results of this study reveal a new paracrine signaling pathway involved in cardiomyocyte hypertrophy and significantly advance our understanding of the role of miR and exosomes in cardiovascular pathophysiology. While our knowledge in this area is still in its infancy, studies such as this highlight the vast potential of exosome-mediated signaling as a therapeutic approach in hypertension and cardiovascular disease.

What did HYVET really tell us?

Bo Carlberg

In the last issue of Journal of Hypertension, Beckett and colleagues report the interesting results from subgroup analyses in HYVET (Hypertension in the Very Old Trial) [1].

In HYVET, old patients (≥80 years, n= 3845) with hypertension were randomized to treatment with perindopril/indapamide or placebo [2]. The treatment goal was a blood pressure < 150/90 mm Hg. Achieved blood pressure was 144/78 mm Hg in the intervention group and 159/84 mm Hg in the placebo group. The study was stopped after a mean of 2 years of follow-up, as the total mortality was higher in the placebo group than in the active treatment group.

The subgroup analyses highlights interesting data. Two thirds of the patients in HYVET were previously treated for hypertension and on third had not been previously treated. Thus, in the majority of patients, the study investigates the effect of stopping treatment, more than initiating treatment. The outcomes in these two different groups of patients are summarized in the table. The effect of treatment on stroke and heart failure were similar in the two groups. However, total mortality and cardiovascular mortality was only reduced in patients with previous treatment. Thus, to replace antihypertensive drugs with placebo in the very old was related to increased mortality. Interestingly, the STOP-1 study, where elderly patients were randomised to treatment with antihypertensive drugs or placebo was also stopped prematurely because of increased mortality in the placebo group [3]. That study also included patients where ongoing treatment was stopped before randomisation.

The issue about initiating treatment vs. stopping treatment has not been analysed in systematic reviews of the effects of antihypertensive treatment in the elderly[4].

- The results from the HYVET study are the most important evidence behind recent guidelines for treatment of hypertension in the very elderly. If most of the data comes from

studying the effect of stopping treatment, a number of new questions have to be addressed.

If it is dangerous to stop antihypertensive treatment in healthy elderly, is it more or less dangerous to stop treatment in frail elderly?

- Should guidelines include advices about stopping antihypertensive treatment in the elderly?
- Should a recommended treatment goal below 150/90 mm Hg be replaced by "not above 150/90 mm Hg"
- Antihypertensive therapy is often reduced or stopped in frail elderly because of side-effects or risk for side-effects. Should this common routine be tested in randomized controlled trials?

References

1 Becket N, Peters R, Leonetti G, Duggan J, Fagard R, Thijs L et al. Subgroup analyses from the hypertension in the very elderly trial (HYVET). J Hypertens 2014; published ahead of print: doi: 10.1097/HJH.0000000000000195

2 Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, et al. Treatment of hypertension in patients 80 years of age, or older. N Engl J Med 2008; 358:1887–1898.

3 Dahlöf B, Lindholm LH, Hansson L, Scherstén B, Ekbom T, Wester PO. Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension). Lancet 1991;338:1281-85.

4 Musini VM, Tejani AM, Bassett K, Wright JM. Pharmacotherapy for hypertension in the elderly. *Cochrane Database of Systematic Reviews* 2009, Issue 4. Art. No.: CD000028. DOI: 10.1002/14651858.CD000028.pub2.

Table 1 Hazard Ratios for treatment with indapamide ± perindopril compared with placebo in patients with or without previous treatment in HYVET.

	Patients with no previous treatment for hypertension Starting treatment vs placebo n=1359 Hazard Ratio (95 % confidence interval)	**Patients with previous treatment for hypertension** Continuing treatment vs placebo (Stoppning treatment) n= 2486 Hazard Ratio (95 % confidence interval)
Mortality	0,95 (0,69-1,31)	0,71 (0,56-0,90)
Cardiovascular death	0,94 (0,61-1,47)	0,69 (0,50-0.97)
All cardiovascular events	0,69 (0,48-0,99)	0,65 (0,50-0,86)
Stroke	0,73 (0,39-1,36)	0,69 (0,44-1,07)
Heart failure	0,28 (0,12-0,65)	0,42 (0,23-0,76)

The Lancet – special hypertension issue for the Hypertension Athens meeting

The International Society of Hypertension (ISH) has had a very good relationship with The Lancet for many years. In 2008 in Berlin, The Lancet Editor, Dr. Richard Horton, was made an honorary member of the ISH and this year in Athens, the same honour will be bestowed on the Journal's fast-track editor, Dr. Stuart Spencer.

Similar to what The Lancet does on cardiology before the annual meetings of the American College of Cardiology (ACC) and the European Society of Cardiology (ESC), there will be special issue on hypertension before the upcoming meeting in Athens; the Journal has kindly provided free copies for all registered delegates, to be found in their congress bags.

Lars H. Lindholm

COUNCIL'S CORNER – HYPERTENSION ISSUES; A PERSONAL VIEW

Aletta E. Schutte

South Africa

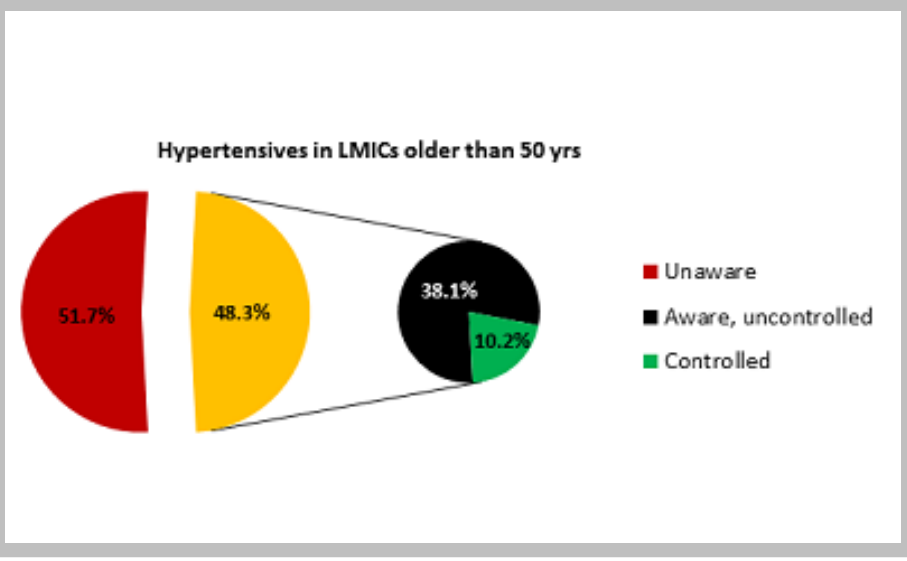
Any *quick fixes* for hypertension out there?

Within the sphere of the ISH one is forced to 'zoom out' from developed countries, and take note of what the impact of hypertension is globally. With the world population running over 7 billion, latest statistics indicate that 83% (5.9 billion) reside in low and middle-income countries (LMICs).[1] It is therefore no wonder that 80% of NCD deaths occurred in developing countries in 2008.[2] Future predictions are all but rosy, indicating e.g. that Africa's population is expected to more than double by 2050.[1]

When living and working in a developing country one is struck by the reality that numerous individuals suffer and die from hypertension-related consequences without ever being aware of their condition. It was shown recently in LMICs that less than 50% of those with hypertension are aware of their condition, with only 10% controlled.[3] The reality is that 90% of hypertensives in LMICs aged over 50 are walking around uncontrolled. We may have highly effective antihypertensive treatment, but we have to face the fact that we are not doing a great job for the majority of the world population.

The international hypertension community becomes excited by innovative and novel technologies that could change the way in which hypertension is treated – as recently seen with renal denervation. The mind-blowing technological era of the space age showed the world that practical spinoffs of high-end technology could end up in numerous advances on ground level, including medical innovations benefitting almost every household in the world. Novel technologies for hypertension treatment may with time hopefully also impact the 5.9 billion in the developing world. But how is it possible that in 2012 there were 6 billion mobile phone subscriptions in the world, of which nearly 5 billion were in developing countries?[4] How is it possible that we can deliver soda drinks and mobile phones to most of the world, but due to dysfunctional health systems, hypertension awareness, prevention, treatment and control remain beyond our reach?
The 25x25 strategy to achieve a 25% relative reduction in overall mortality from NCDs by 2025 is a powerful initiative. But we will reach 2025 in only 10 years, thus the strategy to reach these goals needs to rely on 'best buys' such as secondary prevention and tobacco control. To make a long-term impact we also need to start thinking of novel ways to reach the majority of the globe when health behaviours are formed and fixed – to prevent and to invest in the youth, and to protect them from unhealthy behaviours. (Thirty to 40% of the population in LMICs are aged younger than 15.[1]) When it comes to hypertension there does not seem to be a 'quick fix', but we need a long term investment in health and health systems, and we need to start *now*.

1. Population Reference Bureau 2013. http://www.prb.org/pdf13/2013-population-data-sheet_eng.pdf
2. World Health Organization, *Global Status Report on Noncommunicable Diseases 2010* (Geneva: World Health Organization, 2011).
3. Lloyd-Sherlock *et al*. Hypertension among older adults in low- and middle-income countries: Prevalence, awareness and control. *Int J Epidemiol* 2014; 43:116-128.
4. The World Bank. http://www.worldbank.org/en/news/press-release/2012/07/17/mobile-phone-access-reaches-three-quarters-planets-population



(Adapted from Lloyd-Sherlock et al. 2014 Int J Epidemiol)

Michael A. Weber, MD

Professor of Medicine, State University of New York, Downstate College of Medicine

USA

A Personal View on How The Debate Over Hypertension Guidelines Exposes a Critical Lack of Evidence

Guidelines for the management of hypertension have generally focused on defining and diagnosing this condition as well as setting treatment goals and optimising the use of antihypertensive drugs. Establishing the blood pressure threshold at which hypertension is diagnosed, and to which it should be treated, may be the single most important issue.

Until quite recently there appeared to be a consensus in Europe and the United States: The diagnostic and treatment threshold was 140/90 mmHg for all adults except those with diabetes or chronic kidney disease, in whom 130/80 mmHg was recommended. Then, in 2009, the European Society of Hypertension published a "reappraisal" article acknowledging the absence of definitive data to support the 130/80 mmHg criterion for patients with diabetes or kidney disease and recommending that these patients be treated to 140/90 mmHg like everyone else. Evidence, so it seemed, had become the true foundation for hypertension guidelines.

But this action exposed a larger problem. What evidence justifies a systolic BP of 140 mmHg as the standard threshold for defining hypertension? This is a pivotal question in patients aged over 60 who are so commonly affected by hypertension and in whom most of the serious cardiovascular events occur.

When the ESH/ESC guidelines committee addressed this issue in 2013 they considered two classic hypertension trials, SHEP and Syst-Eur, that studied patients aged 60 or over. But neither trial was designed to compare the effects on cardiovascular outcomes of different BP targets; and, moreover, they were conducted in patients with isolated systolic hypertension, a condition rather different from the hypertension found in the general population. In the end, the Committee, noting that people with systolic BPs above 160 mmHg had clear benefits when treated to below 150 mmHg, recommended a target of 150 mmHg in "frail" older people and 140 mmHg in the "fit."

The guideline in the United States (originally called JNC 8 before the JNC was disbanded by its sponsor, the National Institutes of Health) followed a similar pattern, though it extrapolated even more widely from the SHEP and Syst-Eur trials and simply advocated that 150 mmHg be the threshold in people aged over 60 (though 140 mmHg was maintained for patients with diabetes or kidney disease). Rightly, these authors stressed the absence of definitive data to determine whether 140 or 150 mmHg should be the threshold in these patients, but it was not made entirely clear why 150 mmHg was ultimately recommended.

Indeed, the JNC Committee became strongly divided on this issue and an influential minority of its members published a separate report stating that 140 mmHg would have been a more responsible recommendation. They argued that achieving 140 mmHg is known to be safe, and until it's known that 150 mmHg does not increase cardiovascular risk – especially stroke – it would be more prudent to continue the 140 mmHg standard. Despite this dispute, it should be acknowledged that the JNC panel gave 5 years of dedicated service to evaluating the entirety of the hypertension literature in a search for usable evidence.

The joint guideline of the American Society of Hypertension and the International Society of Hypertension – of which I was an active part - was published at the beginning of 2014. It also noted that the systolic standard of 140 mmHg is not rigorously supported by prospective evidence, but nevertheless recommended it as an expert opinion. Based on the HYVET trial, an exception was made for people aged 80 or more where the evidence for a threshold of 150 mmHg appeared reasonable.

Despite the differences among guidelines, I continue to support the argument that until new research provides further guidance it would be most responsible to remain with the 140 mmHg systolic threshold, if tolerated, in adults aged below 80.

An invitation to attend Society Events, Athens

We invite our members to attend the following events during the forthcoming Hypertension Athens meeting.

ISH General Meeting
Sunday 15th June
12:45-14:15 hrs
Nikos Skalkotas Hall, Megaron Centre

ISH Awards Ceremony, Franz Volhard Lecture and Presidential Lecture
Sunday 15th June
17:00-18:30 hrs
Christos Lambrakis Hall, Megaron Centre

The South African Scenario

Compiled by Brian Rayner

With a contribution from Lionel Opie

Brian Rayner (Left)

Lionel Opie (Right)

South Africa is in the throes of 2 major health epidemics that are on a collision course. Nearly 6 million of the population (approximately 50 million people) are living with HIV/AIDS, and recent statistics show that 30% of the adult population have hypertension. These 2 major epidemics are on collision course, and are stretching the capacity of the South African Health system.

The prevalence of hypertension has risen by 10% in absolute terms and reflects a major deterioration in the lifestyle patterns of South Africans. According to the latest statistics from the Medical Research Council there have been very worrying trends.

South Africa has high levels of physical inactivity – 48% of adult men and 63% of adult women were categorised as inactive. Moreover South Africans are also increasingly eating a typical Western diet comprising increased calorie intake, fat (particularly saturated fat), animal protein and sugar, but a lower intake of unrefined carbohydrate and fibre. There is low intake of fruit and vegetables, and salt intake has also been increasing over this period. About 35% of adult men and 10% of adult women smoke tobacco, and about 16% of adult men report hazardous/harmful use of alcohol with an increase in recent years. More than 70% of women and 45% of men above 35 years old are overweight or obese. Although there are no national data on the trends, there is evidence of increases in the prevalence of diabetes and raised LDL blood cholesterol among urban Africans in Cape Town. The most worrying trend is doubling of the prevalence (now between 11-12%) of hypertension in adolescents aged 15-25 years. This is stretching the resources of referral clinics to investigate the "young hypertensive".

South Africa has recognised the importance of non-communicable diseases (NCDs) and some, but insufficient, progress has been made. In particular, South Africa has been a global leader in adopting legislation for tobacco control, with some signs of an effect. In addition legislation is being mooted to control the content of salt in processed foodstuffs, which accounts for over 60% of non-discretionary salt intake. However the reality is that greater efforts need to be made to address this major epidemic of non-communicable diseases and it definitely is a race against time. There is no doubt the South African public are less interested in chronic diseases like hypertension. Cancer, child health, the latest fad diet and heart disease tends to catch their imagination and their financial contribution. There is a lot to be done in South Africa, and organisations like the South African Hypertension Society, and the Heart and Stroke Foundation are trying to educate the population to the dangers on non-communicable diseases like hypertension. However South Africa is constrained by the number of skilled health professionals with a real interest in NCDs, and promoting the benefits of early detection and management of hypertension.

Finally, from the management perspective, patient management has become increasingly complex with patients having co-existent HIV, hypertension and/or diabetes. There are significant drug interactions between anti-hypertensive drugs and anti-retrovirals (ARVS), the propensity for ARVs to cause metabolic problems and for HIV to cause kidney disease especially in our Black population. There are few specialist Hypertension Clinics in South Africa to assist in managing these complexities.

Events

World Hypertension Day (in May) was marked by blood pressure monitoring sessions conducted by the Heart and Stroke Foundation, and awareness activities were conducted by young researchers from the Hypertension in Africa Research Team (HART).

The South African Hypertension Society (SAHS) is holding their biennial congress in Durban from 22-24 August 2014. There will be a combined event with the Stroke Society because of our mutual interests. We have an exciting programme with 5 international speakers including Prof Bryan Williams from London, Dr David Spence from Canada, Dr Rhian Touyz from Glasgow, Dr Peter Sandercock from Oxford, and Dr Patrik Michel from Lausanne. There will also be a basic workshop for nurse practitioners. International delegates are encouraged to attend and take the opportunity to visit Southern Africa. For further details please visit the website - http://www.strokeandhypertension2014.co.za/.

Guidelines

The South African Hypertension Society has been active in promoting guidelines that are relevant to South Africa. The last Guideline was published in 2011, and the Society is in the process of developing a practice guideline that will be simplified to ensure effective hypertension can be delivered to more South Africans particularly by nurse practitioners.

Awards

Three members of the Southern African Hypertension Society will receive international awards this year. Prof YK Seedat was awarded the **ISH Developing World Award** from the International Society of Hypertension. This is in recognition of lifetime commitment to the promotion of hypertension, his impressive publication record in the field and outstanding work in the developing world, in particular in Africa. Prof Brian Rayner the **Notable Achievement in Hypertension** from the World Hypertension League (WHL) for his work related to his unique finding of a single mutation in the Epithelial Na Channel that was strongly associated with hypertension in South African populations, and responded to amiloride treatment. Prof Krisela Steyn will also honoured for her ground breaking research in promoting salt reduction in indigenous Africans in South Africa and tirelessly engaging the authorities to legislate the content of salt in processed foods. She will receive the 2014 WHL **Notable Achievement in Dietary Salt Reduction Award.**

Research Activities

In South Africa there are 3 majors centres conducting hypertension related research namely:

- **The HART group from the University of North West under the auspices of Prof Rudolph and Prof Alta Schutte**
- **Department of Physiology from the University of Witwatersrand (WITS) under the direction of Prof Gavin Norton and Prof Angela Woodiwiss**
- **The Division of Nephrology and Hypertension from the University of Cape Town (UCT) under the direction of Prof Brian Rayner**

The Hypertension in Africa Research Team (HART) conducts research on the development of hypertension in black South Africans involving epidemiological and clinical research projects. The team consists mainly of physiologists, but also biochemists and nurses, and collaborate with numerous international groups. Within a Hypertension Research and Training Clinic state-of-the-art research measurements are being performed, including echocardiography, retinal microvascular structure and function, 24-h blood pressure monitoring, acute cardiovascular stress reactivity testing and pulse wave velocity. Involvement in multi-national studies such as the PURE study pave the way for the group being able to report on the development of hypertension and the consequences thereof in a sample of 2000 black individuals. Several high-impact papers have been published in international journals in recent years, with all team members focusing on the epidemiology of health behaviours but also detailed aspects of cardiovascular structure and function to understand disease development (such as the role of oxidative stress and nitric oxide bioavailability, psychological distress and coping mechanisms, haemostasis, HIV-infection and its treatment).

The WITS group research activities centre around the cardiovascular effects of hypertension, genetics of hypertension, and blood pressure monitoring amongst many other research interests.

The Cape Town group research activities concentrate on the genetics of salt sensitivity and salt sensitive hypertension in indigenous populations, ACE inhibitor angioedema, blood pressure monitoring in patients with HIV, therapeutic monitoring, the effects of amphetamine abuse, physiological treatment of hypertension and the effects of vascular calcification on central BP in patients with chronic kidney disease. Future research will be focused on the effects of the collision of the HIV and NCD epidemics.
Research activity in South Africa is severely constrained by lack of access to significant research funding.

Conclusions

South African Health services are severely constrained by the impact of 2 major epidemics namely HIV and NCDs. Despite efforts to contain the effects of poor lifestyle the effects continue to have a major effect on the prevalence of hypertension, which has risen by 10% in absolute terms. South Africa is constrained by the shortage of trained professionals, lack of access to clinics and limited money for research. There needs to be a greater urgency from government and non-governmental organisations to address the impact of NCDs on the health of South Africans.

Activities conducted by the HART group on World Hypertension Day, 2014.

ISH International Forum News

The ISH International Forum is an important grouping of national and regional societies in hypertension and related cardiovascular conditions.

They form a special link between their own members and the ISH and facilitate 2-way communication of ideas and plans to further mutual goals. Every second year at our Scientific Congress there is an opportunity for Forum members to meet face-to-face and discuss activities and developments in the preceding 2 years, while looking ahead to new projects of broad significance.

This year the Forum will convene in Athens on Saturday 14 June at 12:45 PM.

We are looking forward to updates from several Forum members regarding local activities. There will be a special discussion and presentation from Dr Norman Campbell, President of the World Hypertension League (WHL). There are many bonds that link the WHL and the ISH Forum and the success of joint projects will exemplify how we can work closely together. In particular, the production and release of WHL/ISH recommendations regarding sodium and a fact sheet regarding hypertension are two achievements of direct relevance and utility to local and regional societies in their interactions with the public and government.

We are looking forward to a stimulating meeting and we would encourage each of the ISH Forum members to be represented on the day.

Stephen Harrap
ISH Forum Officer

Join us at the ISH International Forum meeting in Athens!

New Investigator Committee (NIC) Update

Athens ISH New Investigator Meeting Programme

An ISH New Investigator Meeting Programme has been integrated into the Hypertension Athens meeting as follows.

1. ISH NIC Oral Presentation session (June 14th- 09:00-11:00 hrs)

- Featuring oral presentations of top scoring abstracts from new investigators.
- A Keynote presentation from Professor Stephen Harrap. **'Blood Pressure Research - Looking Back, Looking Forward'.** This promises to be an exciting and enlightening lecture from the former ISH President.

- A special **'Quizzing the Lancet Editor'** feature with Dr. Stuart Spencer where participants will have the opportunity to ask questions about the peer review process of one of the highest impact journals in biomedical research.

2. ISH Austin Doyle session (June 15th- 09:00-11:00 hrs)

A joint presentation by the ISH Awards Committee and the ISH New Investigator Committee. Established in honour of Austin Doyle, past ISH president and founding chairman of the High Blood Pressure Research Council of Australia this award is a true highlight of the ISH Scientific Meeting.

3. ISH NIC Poster Presentation session (June 14th 14:00-15:30)

Featuring top scoring abstracts presented by new investigators in basic, clinical, and population research in hypertension.

4. ISH New Investigator Networking Event - as detailed above

5. ISH New Investigator Committee Media Coverage

As always the New Investigator Committee will be providing real time updates on sessions through Twitter, and will feature video interviews with award winners and senior scientists.

San Francisco, ISH New Investigator Symposia - 8th September

A further half day ISH New Investigator Symposium will take place on 8th September 2014 at the time of the Council of High Blood Pressure Research (CHBPR) of the American Heart Association Scientific Sessions.

Highlights of this event will again include:

- Keynote speaker
- Awards for the best oral and poster presentations
- Free registration
- Evening social event

Abstracts for this event will be submitted independently of the CHBPR Meeting and further information will be issued shortly in this regard.

Report of the ISH Support of the Vietnam Hypertension Society Meeting & Initiatives

17 – 18 May 2014

Trefor Morgan

The Vietnam Society of Hypertension held its inaugural meeting in Hue, Vietnam on May 17 and 18 at the Indochine Palace Hotel, Hue. The dates were chosen so that the meeting was held on World Hypertension Day and activities were organised to involve the community and to make them aware of Hypertension. The impetus to holding this meeting was partially due to the offer of support from the International Society of Hypertension to sponsor two speakers to attend the meeting. An important aspect of support from ISH for activities in the Asia Pacific region is that the host society must bear responsibility for internal costs associated with the visit.

The meeting was attended by over 800 delegates from all regions of Vietnam and was preceded by a CME course on Hypertension on the preceding day. This was held at Hue Medical University which is responsible for training doctors and other medical personnel for the Central part of Vietnam, population 26 million. The CME course was attended by 120 participants. After the lectures an assessment wasperformed so that appropriate points were gained. Trefor Morgan spoke at the CME course on **Ambulatory Blood Pressure Why?** The talk was well received and many questions were asked.

The Main conference was held on May 17 and consisted of two parallel streams. One related more to epidemiology and importance of hypertension the other to practical issues in management.

PROGRAMME

Friday 16 May 2014

08:00-16:00 CME IN HYPERTENSION

Inaugural Meeting of Vietnam Society of Hypertension
Protection and Prevention of Hypertension; From Consensus to Action, For a World without Hypertension".

- Prof. Cao Ngoc Thanh, MD, PhD PhD Dean, Hue University of Med. & Pharm, Co-Chairman, Organizing Committee
- Prof. Pham gia Khai, MD, PhD President, Vietnam Society of Cardiology
- Prof. Huynh van Minh, MD, President, Vietnam Society of Hypertension, Chairman, Organizing Committee

Saturday 17 May 2014

07:30-08:15 OPENING CEREMONY

08:15-10:00	
Hall A	HTN epidemiology in Vietnam and in the world - 2014 HTN guideline
Hall B	Resistant HTN & Emergency
10:15-11:30	
Hall A	HTN prevention
Hall B	HTN in pregnancy and in infant
11:30-13:00	
Hall A	Satellite Symposium sponsored by Menarini
Hall B	Satellite Symposium sponsored by Abbott
13:30-15:00	
Hall A	HTN & Acute Coronary Syndrome complications

15:00-16:30	
Hall A	HTN & cardio-renal complications
Hall B	HTN & Endocrinology disease- Diabetes mellitus
16:30 - 18:00	
	Satellite Symposium sponsored by Merck

18:30 -21:00 GALA DINNER

Sunday 18 May 2014
07:00 - 09:00 Walking parade for Hypertension (Hue University of Med. & Pharm.)

Apart from the talks by Professor Schiffrin and Professor Morgan all proceedings were in Vietnamese thus my comments on the rest of the program are not necessarily accurate. However, there seemed to be much enthusiasm by the speakers and participants with many questions. While some talks were reviews of the topic there were also the results of a number of studies presented.

Teaching Faculty member talks were given in English with slides translated into Vietnamese. Questions were asked in Vietnamese and translated for faculty members. Professor Morgan spoke on the "Importance of Hypertension in Vietnam and the World, Primary Prevention and Nondrug Management", and "Sleep Blood Pressure." Professor Schiffrin spoke on "Modern Management of Hypertension, Use of the Guideline", "Pharmacological Treatment of Hypertension", and "Resistant Hypertension ISH view". All talks generated a large amount of interest and were well received.

On Sunday May 18 there were public activities in which teaching faculty members took part. The students of the University showed great enthusiasm and participation. There was an outreach to the community with blood pressure measurement and risk assessment.

The inaugural meeting of the Vietnam Society of Hypertension was a great success and augers well for its future. We look forward to their members joining the ISH and participating in our Society.

Medtronic, Inc response:

Wendy Dougherty, Director, Corporate Communications

Opus 36 contributions / April 2014 Hypertension News

In reading the April ISH newsletter we were pleased to see the focus on renal denervation and commentary from noteworthy leaders in the field. We did, however, notice a few inaccurate statements in the articles.

Resistant hypertension and renal denervation: Who's kidding whom?
By Peter Sever; pgs. 2-4

- (pg. 3, column 2) Regarding the statement "Symplicity HTN-3 was prematurely stopped because the trial failed to meet its primary endpoint;" SYMPLICITY HTN-3 was not stopped prematurely, and follow up will continue as planned out to five years. The trial was powered for 530 patients and actually enrolled 535. [Indeed, the independent trial DMC did not recommend stopping the trial at any time for safety or for efficacy.]

- (pg. 4, column 1) Regarding the comment, "The device companies have voted with their feet and ceased development and marketing of newer catheters for RDN;" we are aware of only one company announcement to this effect. Many device companies, including Medtronic, are continuing to develop new RDN catheters. Medtronic has received CE Mark in Europe and TGA listing in Australia for its multi-electrode catheter and is continuing to market the product in these regions.

Renal Denervation: Full steam ahead or proceed with caution By Dr. George Bakris, pgs. 5-6

- (pg. 5, column 2) Regarding the statement "SYMPLICITY HTN-1 and SYMPLICITY HTN-2 combined studied less than 200 patients;" in fact there were more than 250 patients between the two studies (153 patients were studied in HTN-1; 106 patients in HTN-2)

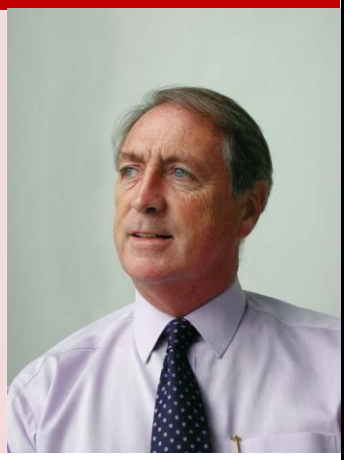
- (pg. 6, column 1) Similarly, the comparison of the size of SYMPLICITY HTN-3 to previous studies in paragraph 2 is overestimated - HTN-3 is less than 4X larger than previous studies (not greater than 4X), considering HTN-1 included 153 patients.

Who's kidding whom or, in search of the truth?

Peter Sever

International Centre for Circulatory Health, Imperial College London

8th May 2014



The author acknowledges the response of Medtronic to his earlier commentary (Hypertension News – Opus 36).

Early reports suggested that Symplicity 3 was stopped prematurely. In the event the trial went to completion, as planned. This does not alter my assessment of the trial and the views expressed. To date, my understanding is that one company has withdrawn from new catheter developments and we await further news from others.

Rarely in the recent history of hypertension research and treatment has there been so much excitement over a novel intervention, namely the introduction of renal nerve denervation (RDN) for resistant hypertension, and the results of preliminary observational studies showing remarkable benefits in BP reduction.

The dismay that accompanied the results of the first properly randomized, blinded, sham controlled trial which dashed all expectations (except in a few quarters!) not surprisingly lead to a raft of explanations as to why the results of the trial were wrong and that the earlier benefits that were reported were representative of the real world!

Almost simultaneous with the release of the Symplicity 3 results was the dissemination of "global" trial results by Medtronic on 1000 patients in the real world, undergoing renal denervation in a totally uncontrolled setting. The implication of these findings and the communication disseminated to untold numbers of physicians (in their thousands?) was that there was something wrong with the design and execution of Symplicity 3, and that in the real world things were different, and that the technique was effective and a real solution to the problem of resistant hypertension.

My first response to this is that it challenges the basic concept in clinical medicine that the truth can only be guaranteed following the conduct of the gold standard randomized double blind, controlled clinical trial. That the failure of Symplicity 3 to demonstrate benefit was due to failure of denervation or patient selection, seems highly improbable. Unlike the observational studies, patients had to be on maximum doses of 3 or more drugs, had ABPM to confirm established resistant hypertension, and were a more heterogeneous population, particularly with reference to ethnicity. If the negative outcome of Symplicity 3 was due to incomplete denervation or some technical problem with the procedure, then given the magnitude of blood pressure lowering in the earlier trials, if a true finding, then 75% or more of the denervations in Symplicity 3 would have to have failed. Is that really likely?

The alternative suggestion is that the results were confounded by the high representation of black patients in whom the pathophysiology of resistant hypertension might be different, and therefore less responsive to renal denervation.

I don't really like this suggestion either. Do we really dichotomize the hypertensive population so simplistically into black and white? I accept that volume dependent mechanisms might prevail to a greater extent in black hypertensives, but if all patients recruited into Symplicity 3 had optimal doses of diuretics and many had had a trial of spironolactone, then differences between ethnic groups should have been minimized.
Let's take a lesson from the real world of clinical medicine, and reflect on the ongoing saga of statin induced myalgia, which in observational studies, some claim, is seen in 10% or more of statin users. Interesting, when in blinded randomized placebo controlled trials (CT), you can't tell who is on a statin and who is on placebo. For such a dramatic difference between a CT and observational studies what is the explanation? Let me suggest to you that in this case it is expectation.

Such is the widely promoted and popularized view about statins that all potential users "know "there may be muscular side effects. However note the recent study of statin associated myalgia… symptom resolution on withdrawal of statin and recurrence of symptoms in 80% of patients on rechallenge. Impressive eh! Problem was rechallenge was with placebo.

So back to RDN. I have already demonstrated that the vast majority of patients with resistant hypertension don't take their drugs (see April 2014ISH Hypertension News commentary). In the context of this quite dramatic intervention procedure (sham or real), with intensive follow there is a real likelihood that compliance improves in both groups. Isn't that the most likely explanation for the results of Symplicity 3?

So before we make excuses for Symplicity 3 and advocate continuing in the real world with ongoing RDN procedures and national registries which, in my opinion, is totally wrong and will only perpetuate the myth that RDN is a magic cure for resistant hypertension, we, as scientists and clinicians, demand a further well controlled trial, independently sponsored, with full work up of patients ,including optimisation of drug treatment, compliance assessment by observed drug ingestion and urine drug analyses and, if necessary, stratified by ethnicity (and let's not forget there are more than two ethnic groups

with resistant hypertension!). BUT, like Symplicity 3, it will be sham controlled and blinded.
Then we will see the truth.

I would love RDN to work. The rationale and the background science is all entirely plausible. However, to date, we are still at the stage where the emperor has no clothes (see earlier ISH report – April 2014 issue). Let's see if Symplicity 4 can put his clothes back on!

ODD CORNER FROM THE LANCET

THE CASE OF GEORGE EDALJI: A QUESTION FOR OPHTHALMOLOGISTS.

To the Editors of THE LANCET.

SIRS,—Might I ask you in the cause of justice to permit me to put the following question to those of your readers who are engaged in eye practice:—

"Do you consider it physically possible for Mr. George Edalji, whose degree of myopic astigmatism as determined by retinoscopy under homatropine is

Right eye – 8·75 diop. spher.
– 1·75 diop. cylind. axis 90°.
Left eye – 8·25 diop. spher.,

to have set forth upon a pitch dark night with neither moon nor stars, to have crossed country for half a mile climbing fences, finding gaps in hedges, and passing over a broad railway line, to have found and mutilated a pony which was loose in a large field, to have returned half a mile, and to have accomplished it all under 35 minutes, the limit of the the possible time at his disposal? Mr. Edalji did not wear spectacles."

A consensus of scientific opinion upon this point would greatly aid me in getting justice for this young professional man, condemned for an offence which in my opinion he could not possibly have committed.

I am, Sirs, yours faithfully,
ARTHUR CONAN DOYLE, M.D.

Undershaw, Hindhead, Surrey, Jan. 13th, 1907.

THE LANCET,] [JAN. 19, 1907.

WORLD HYPERTENSION DAY (WHD) 2014: 17 MAY

WORLD HYPERTENSION DAY
Initiated by the World Hypertension League

To mark WHD, the ISH New Investigator Committee Media Working Group compiled a video entitled
'I Stand Against Hypertension'.
http://ish-world.com/new-investigators-casts/

Three posters were also created for use by ISH members during 2014 World Hypertension Day initiatives. These were kindly translated into Spanish and Portuguese by International Forum colleagues.

Please view the WHD posters, as well as member and Society WHD reports at www.ish-world.com.

MEMBERSHIP INFORMATION

ISH Secretariat New Contact Details

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

ISH Secretariat

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Delivering Excellence in Event Management

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ISH Registered Charity No: 1122135

Membership subscriptions 2014

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

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

Please contact the Secretariat to receive a payment form.

Please help us to recruit new members

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

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

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

ISH CORPORATE MEMBERS

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