

# HYPERTENSION NEWS

April 2014, Opus 36



## IMPORTANT MESSAGE FROM THE ISH PRESIDENT

Ernesto Schiffrin, MD, PhD,



## ISH transfers to a new service provider, The Conference Collective



After many years of having our affairs managed by Hampton Medical Conferences, for reasons of efficiency, the Executive decided to transfer its contract for services to the Society to The Conference Collective, another UK-based service provider with an excellent reputation. Some of you may remember Mrs. Jacinta Scannell, who used to work for Hampton Medical Conferences until a few years ago. She is the Director of The Conference Collective and has offered very favourable terms to ISH, and a number of services and support that were not available with our previous service provider.

We are lucky that Mrs. Helen Horsfield, who managed our Secretariat for Hampton Medical Conferences, is also transferring to The Conference Collective. We have always received excellent support from Helen, and in the past from Jacinta, so we are confident that ISH will continue to have superb management of its activities.

Our contract with The Conference Collective started on April 1, 2014, but our agreement with Hampton will continue until later in the year to facilitate the transfer of activities from one organisation to the other. So from now onwards, you should not be surprised to receive ISH correspondence coming from The Conference Collective, but continuing to be managed by Helen.

We thank Hampton Medical Conferences for the years that they provided their service to us, and look forward to working with The Conference Collective and with Helen for the foreseeable future.



Jacinta  
Scannell



Helen  
Horsfield

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Join us at the Hypertension Athens meeting in June!

[www.hypertension2014.org](http://www.hypertension2014.org)

## NOTES FROM THE EDITOR

Dear ISH member

**Renal denervation -  
how did it get  
accepted so  
uncritically?**

Lars H. Lindholm



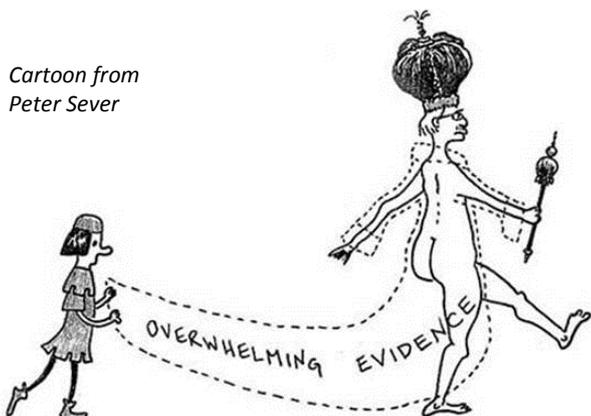
In this issue of Hypertension News, three distinguished hypertension specialists have been invited to present their views on renal denervation in general and the negative outcome of the Symplicity 3 study in particular. First, Peter Sever's expresses his views with the (shortened) title "Who is kidding whom?" Second, George Bakris (the senior author of the Symplicity 3 paper) follows with "Full steam ahead or proceed with caution"? Third, Murray Esler's defends the technique in a paper entitled "Has a beautiful idea been ruined by cold, hard facts?"

Several things stand out: First - and a strong argument from Peter Sever - did the patients really have resistant hypertension or were they just badly controlled before the trial and got the right treatment when they were included in a complicated trial. Second - as Murray Esler and George Bakris comment - were the patients really denervated or were some of the operators too inexperienced to perform the procedure correctly? Third, how could renal denervation get into clinical practice before results of properly controlled trials had been attained? We all know how difficult it is to get a new drug registered.....

**So where do we go from here?** The renal denervation technique should not be abandoned but be further investigated in clinical trials where one is assured that the patients take their medications and that renal denervation really takes place.

Lars H Lindholm, Editor

Cartoon from  
Peter Sever

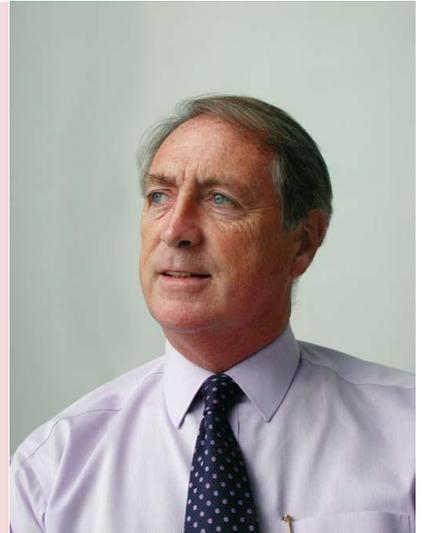


## Hot off the Press A FOCUS ON RENAL DENERVATION

### Resistant hypertension and renal denervation: Who's kidding whom?

Peter Sever

International  
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Imperial  
College London



Resistant hypertension is defined as blood pressure remaining above goal in spite of the concurrent use of 3 antihypertensive agents of different classes. Ideally one of these agents should be a diuretic and all agents should be prescribed at optimal doses. Its true prevalence is unknown but observational studies and clinical trials suggest that it is a common clinical problem. In an analysis of National Health and Nutrition Examination Survey (NHANES) (1), of participants being treated for hypertension only 53% were controlled to a blood pressure <140/90 mm Hg. In those with diabetes or chronic kidney disease the percentage controlled was considerably less. Similar figures (63%) for all treated patients have recently been reported by the Health Survey for England (2) but, of course, many of the participants in these surveys were not receiving optimal treatment for their hypertension.

Resistant hypertension comprises a heterogeneous group of patients including those with undiagnosed secondary hypertension, inaccurate blood pressure measurement, white coat hypertension and poor adherence with prescribed medication. In the author's experience true resistant hypertension is uncommon. Thus, in the evaluation of patients with apparent resistant hypertension, a comprehensive management algorithm should be applied which includes investigations to rule out secondary causes, confirmation of appropriate treatment (drugs and doses), including a trial of spironolactone, and formal assessment of drug compliance. This should include observed drug ingestion in the clinic followed by blood

pressure monitoring for up to 4 hours and 24 hour ambulatory blood pressure monitoring thereafter. The post-dosing period of observation for 4 hours in the clinic is a precaution for cases where substantial falls in blood pressure occur in the hitherto non-compliant or poorly compliant patient. If the facility is available, urinary drug assays provide additional information on non-compliance.

Only after the diligent exclusion of the majority of patients referred with so-called resistant hypertension can true resistant hypertension be diagnosed with confidence.

In a series of 35 patients referred to a specialist clinic, all of whom claimed to be taking their medications as prescribed, and in whom secondary causes for their hypertension had been eliminated and optimal treatment, including a trial of spironolactone, had been prescribed, following observed drug ingestion and 24 hour ABPM, 60% achieved a blood pressure of <140/90 mm Hg and 80% <150/90 mm Hg (3). The original series has now been extended to over 100 patients and the outcomes will shortly be available.

It is therefore manifest that poor drug compliance is the major contributing factor to apparent resistant hypertension and without its systematic evaluation, resistant hypertension will be grossly over-diagnosed.

It is against this background that we can now look at the history of trials of renal denervation (RDN). In both Symplicity HTN-1 (an uncontrolled study)(4) and Symplicity HTN-2 (a non-intervention controlled study)(5), impressive reductions of clinic blood pressure (circa 30 mm Hg systolic) were reported following RDN, and these reductions maintained during extended follow up for up to 3 years. Other European Centres have reported similar impressive reductions in blood pressure in uncontrolled studies (6), and two meta-analyses have been published (7,8). In general the technique has been uncritically accepted and practiced worldwide. Specialist centres, including the author's, receive weekly referrals from practicing physicians for consideration of RDN in apparent treatment resistant hypertension. Against the "hype" surrounding RDN there have been few words of caution.

None of the Symplicity studies screened patients for non- or poor compliance. Only one in five had received a trial of spironolactone, which in our experience has been shown to produce falls in blood pressure almost as great as those seen with RDN (9). In Symplicity HTN 2, the reduction in blood pressure with ABPM following RDN was only 11/7 mm Hg, a far smaller reduction than one would have anticipated from the clinic recordings. As Howard and colleagues have pointed out (10), in drug trials without randomisation or blinding, clinic blood pressure reductions are substantially greater than reductions in blood pressure as assessed by ABPM. However, with randomisation and blinding, reductions as measured in the clinic and by ABPM are remarkably similar. These authors predicted that this would be the case with the first randomised, controlled, sham operated trial of

RDN, Symplicity HTN 3, with an effect size nearer to 10mm Hg than 30 mm Hg systolic pressure.

Interestingly, Fadl Elmula and colleagues have reported, in a small series of patients undergoing RDN with treatment resistant hypertension after witnessed intake of medication and ABPM, that no fall in either clinic or ABPM blood pressures followed RDN (11). In a subsequent paper the same authors report that, after excluding poor drug compliance, adjusting drug treatment was more effective than RDN in lowering blood pressure in true resistant hypertension (12). Whilst many have urged caution over the widespread and often uncritical application of RDN to suspected cases of resistant hypertension, the technique has been extensively adopted by cardiologists and interventional radiologists in many countries, with a proliferation of device manufacturers entering an anticipated rapidly expanding and lucrative market. Guidelines on the application of RDN for the treatment of resistant hypertension have been published by the British Hypertension Society (13) and other organisations (14), but the strict criteria recommended prior to qualification for RDN have, in international practice, almost certainly not been adopted.

Symplicity HTN-3 was prematurely stopped because the trial failed to meet its primary endpoint, the change in office systolic blood pressure from baseline to 6 months (15). The difference in systolic pressure between the intervention arm and the sham operated arm being only 2 mm Hg systolic pressure. Obviously a far less impressive outcome than many would have anticipated from the earlier observational and non-sham controlled trials. The authors, however, confirmed that the procedure was safe, with few complications- an outcome similar to other earlier trials of RDN.

It has previously been suggested that substantial reductions in blood pressure in previous RDN trials could have been explained by better adherence to drug therapy following the procedure, during intensive follow up under close observation by physicians (16). Without doubt, from our observations in patients with resistant hypertension, and from studies of urine drug concentrations, compliance with medications is a major problem in this group of patients. It is entirely possible that in the context of a formal trial, particularly when RDN is controlled by a group undergoing a sham procedure, that improved compliance with drug taking post procedure would be similar in the two groups.

The possibility, in Symplicity HTN-3, that RDN was ineffective in the trial, compared with sham operation, because of inadequacies in the denervation procedure is extremely unlikely. The technique is relatively simple, and those participating in the trial will have been appropriately trained in its conduct.

So what of the future?

The scientific background and the work leading up to RDN was sound, and the innovative work of Esler and colleagues commendable (17). The early trials of RDN in man certainly reawakened interest in the role of

the sympathetic nervous system in the pathophysiology of hypertension in general and, more specifically, in resistant hypertension. Following Symplicity HTN-3, however, we need to take a big step backwards to re-evaluate RDN. The Joint UK Societies have recommended a moratorium on RDN until the Symplicity HTN-3 outcomes have been appropriately analysed and digested (18). The device companies have voted with their feet and ceased development and marketing of newer catheters for RDN. In my opinion we need a further trial with a larger number of subjects than that reported by Fadl Elmula, where inclusion is restricted to those who are found to be truly treatment resistant after evaluation following observed drug ingestion. Only when such a study has been conducted can we begin to establish the future role of RDN.

This whole episode in the history of hypertension management raises interesting issues, the first being the necessity for properly controlled randomised clinical trials to be carried out prior to the widespread and uncritical uptake of RDN in clinical practice. This would be required for any new antihypertensive drug, so why would we not demand that similar stringent processes are adopted prior to the introduction of a novel blood pressure -lowering device. (This should apply to other devices and proposed methods to treat resistant hypertension that are currently being developed). The second, is the recognition of the enormous problem of poor compliance with drug therapy in hypertensive patients. The cost of poor compliance to health providers is substantial, not only from the wastage of drugs, but the need for more clinic visits, repeated investigations and the morbidity and mortality associated with uncontrolled blood pressure. Drug assays on urine samples are inexpensive and cost effective and expose poor compliance. They should be used routinely in the work up of patients with resistant hypertension.

There may, ultimately, be a place for RDN where drug taking is problematic due to side effects or other causes of non-compliance but further controlled trials in such subgroups would be mandatory.

The natural history of RDN mimics the teaching to many generations of British medical students, on new drugs, by the late Desmond Lawrence - unrivalled enthusiasm, followed by total rejection and then an ultimate place for use in a restricted number of patients. (Figure).

Let us not forget that other interventional procedures in medicine, such as tonsillectomy and knee arthroscopy with washout, have ultimately been shown to be of little value when objectively evaluated.

**On the basis of the evidence to date, therefore, I put the following question to both the physicians and their patients with “resistant” hypertension - Who’s kidding whom?**

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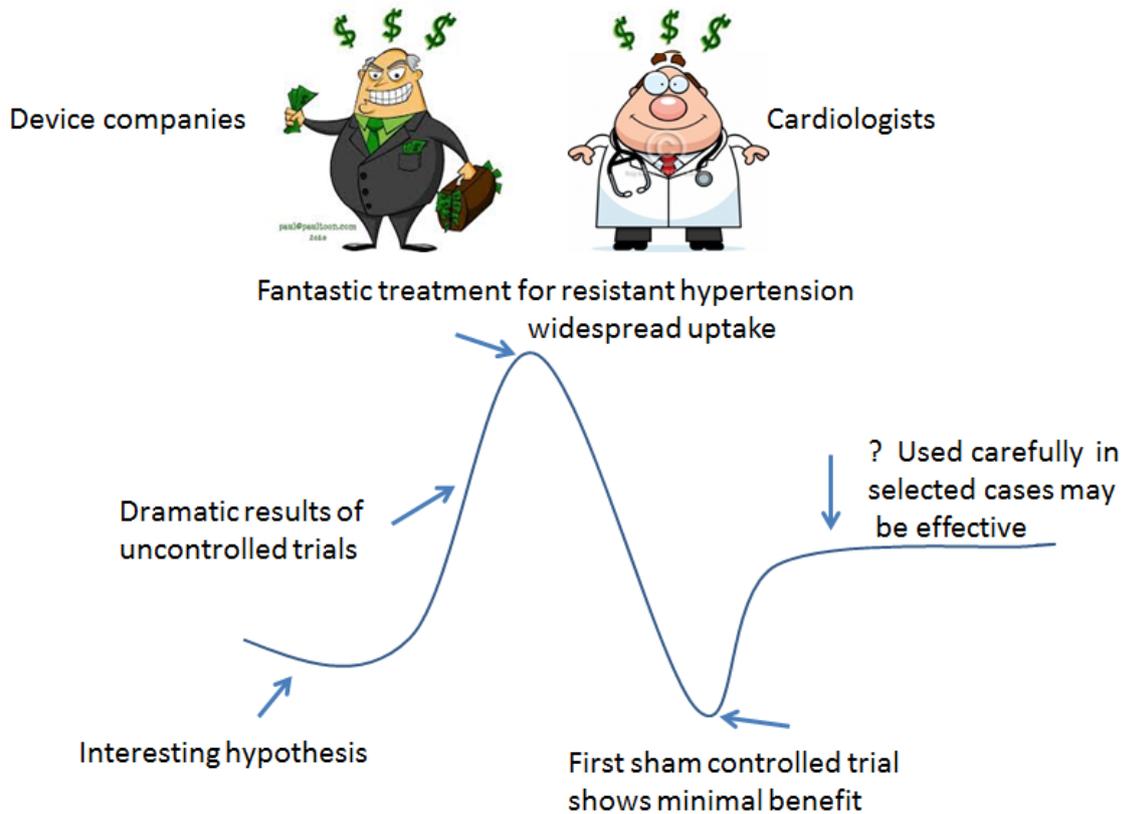
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*Below: Based on a cartoon of the uptake of new drugs by Desmond Lawrence*



### Oscillations in the development of renal denervation

## Renal Denervation: Full steam ahead or proceed with caution

**George Bakris, MD**  
Professor of Medicine and Director, ASH Comprehensive Hypertension Center, The University of Chicago Medicine



Over the past decade there has been great enthusiasm for use of renal denervation as a method of achieving blood pressure control when conventional antihypertensive medications have failed. Early studies provided evidence for proof of concept demonstrating renal denervation clearly reduces norepinephrine spillover and muscle sympathetic nerve activity in people who were defined as having resistant hypertension. Resistant hypertension was defined as being on 3 or more antihypertensive agents with pharmacologically complementary mechanisms of action. This would include a thiazide-like diuretic, blocker of the renin angiotensin system and a calcium antagonist, for example.

The early studies of SYMPPLICITY HTN-1 and SYMPPLICITY HTN-2 combined studied less than 200 patients. Moreover, there were no sham or blinded control arms in these studies nor was there a measure of sympathetic activity with NE spillover or other routine technique before or after the procedure to assess whether complete denervation did indeed occur.

Based on BP outcome data from these studies, however, and the need to expand this procedure into

the United States, the SYMPLICITY HTN-3 trial was commissioned with protocol development involving Dr. Deepak Bhatt and myself as well as key clinical and statistical expertise from Medtronic clinical group. In writing the protocol we wanted to make it as scientifically sound as possible and try to address problems documented with previous protocols such as lack of a sham control group, failure to assess ABPM in all subjects and other related problems. Thus, while the inclusion criteria were generally similar to the previous studies, however, the rigor of documentation for entry was far stricter.

There were key differences of SYMPLICITY HTN-3 from previous SYMPLICITY trials including: a) adding a sham procedure, b) adding patient blinding, c) adding blinding of follow-up assessors, d) blinding of study management, e) adding a baseline ABPM  $\geq 135$  mm Hg as an inclusion criteria as well as pre-specified secondary endpoint of ABPM systolic BP difference between groups. Additionally, SYMPLICITY HTN-3 was  $>4X$  larger than previous trials- 80% powered on a safety endpoint,  $>95\%$  powered for efficacy. This was also conducted with greater rigor and oversight than previous studies.

The results of this prospective, single-blind, randomized, sham-controlled trial carried out in 535 patients was negative. The mean ( $\pm SD$ ) change in the office systolic blood pressure at 6 months, the primary endpoint, was a reduction from a baseline of 180 mm Hg by  $-14.13 \pm 23.93$  mm Hg in the denervation group compared to  $-11.74 \pm 25.94$  mm Hg in the sham-procedure group. While there was no difference between groups, both groups demonstrated a significant ( $P < 0.001$ ) BP reduction from baseline.

The change in 24-hour ambulatory systolic blood pressure, a pre-specified secondary endpoint, was  $-6.75 \pm 15.11$  mm Hg in the denervation group and  $-4.79 \pm 17.25$  mm Hg in the sham group, for a difference of  $-1.96$  mm Hg (95% CI,  $-4.97$  to  $1.06$ ;  $P = 0.98$ ). There were no significant differences in safety between the two groups. Thus, the results of SYMPLICITY HTN-3, a blinded trial, did not show a significant reduction of office systolic pressure or 24 hour systolic ABPM in patients with resistant hypertension 6 months after renal artery denervation as compared with a sham control.

The results of SYMPLICITY HTN-3 are clearly different from previous trials. The reasons for these results are unclear. There are however, a few possible explanations for this variance among trials. First, since there was no specific assessment of denervation it is possible that proper denervation was not accomplished at all sites. It is unclear how plausible this argument is, since all investigators were proctored during each of the procedures. Another explanation is the Hawthorne effect, with many participants now taking their medications. Perhaps in previous studies people did not take their antihypertensive medications which may then enhance the effect of denervation. What is clear is that SYMPLICITY HTN-3 opens the door to more questions rather than closing the door on any further research.

Questions such as how to properly assess whether adequate denervation occurred, where the most concentrated area of nerves in the artery is and how many “burns” are needed for effective denervation are not totally known at this time. Also most patients do not take their BP lowering medications as prescribed and at least one study documents  $<50\%$  of patients actually take their meds when metabolites were measured. Hence, a new chapter begins in renal denervation, thus, as Shakespeare said what has happened is a prologue and we are starting to write chapter 1. Thus, we will proceed with caution.

## Renal denervation in 2014: “Has a beautiful idea been ruined by cold, hard facts?”

**Murray Esler MBBS PhD FRACP**

Senior Director, Baker IDI Heart and  
Diabetes Institute, Melbourne



Renal denervation for hypertension has a long pedigree. In the 1940s widespread surgical sympathectomy was performed, in the era before the advent of antihypertensive drugs, as the first effective treatment for severe hypertension, but with a substantial burden of disabling side effects. At this time no theory identified the sympathetic nerves of the kidneys as pivotal in the pathogenesis of hypertension, but the procedures performed no doubt often sectioned postganglionic sympathetic fibres directed to the kidneys. Subsequent surgical sectioning of the renal sympathetic nerves in animals with experimental hypertension demonstrated their prime importance in pathogenesis, and the work of my group showed that there is preferential activation of the renal sympathetic outflow in patients with essential hypertension, this becoming the therapeutic target with selective renal denervation therapy. Importantly, the renal sympathetic outflow is markedly activated in drug-resistant essential hypertension.

The renal sympathetic nerves pass to the kidneys in the adventitia of the renal arteries, or just outside in perirenal adipose tissue, within reach of radiofrequency or ultrasound energy released in the renal artery lumen. This new therapy has been applied world-wide in approximately 10,000 patients with severe drug-resistant essential hypertension. Multiple studies strongly suggest the efficacy and safety of catheter-based renal denervation, although there are discordant findings, and reports that the response rate is less than the 70-85% reported in the Simplicity trials. In my own tertiary care hypertension clinical practice, many of my previously most challenging severely hypertensive patients now have normal blood pressure subsequent to renal denervation, although usually still also requiring multi-drug antihypertensive therapy.

A challenge to the percutaneous renal denervation treatment of resistant hypertension came on 9 January 2014 with a press release concerning the Simplicity HTN-3 trial in drug-resistant hypertension, the pivotal study for US FDA licensure, indicating that the primary efficacy endpoint had not been reached in the trial. This is a comprehensive, rigorously designed study, so the negative finding will be influential. Screening with 24-hour ambulatory blood pressure monitoring excluded patients with white coat hypertension. The study was blinded, with a 2:1 active denervation: sham procedure design. But there is an Achilles heel with most clinical trials of renal denervation for hypertension, including this one. Whether renal denervation was actually achieved in individual patients was not evaluated in Simplicity HTN-3. For such an otherwise meticulously designed trial this is a noteworthy deficiency, especially as unlike in Australian and European renal denervation trials, the majority of participating interventionists, although experienced in other procedures, had never performed a percutaneous renal denervation; their learning curve fell within the trial.

When it has been documented (as it was in the Simplicity HTN-1 study with renal noradrenaline spillover measurements), the degree of renal denervation achieved with catheter-based renal sympathetic ablation, on average approximately 50%, is substantially less than with experimental surgical denervation (90-95%). Perhaps the usually less than complete denervation has been compounded in Simplicity HTN-3 by operator inexperience. In this context it is pertinent to ask whether current catheter designs and energy delivery are optimal. Should we be aiming for more complete renal denervation? Are some sympathetic nerves, perhaps, more distant from the lumen of the renal arteries than is generally believed, so that deeper penetration of ablating energy is needed? It should be noted that the field of renal denervation for experimental hypertension is

active, in fact energized by the clinical studies. Experimental surgical denervation for hypertension still works!

It has been suggested that inclusion of blinding in Simplicity HTN-3 was the critical element. Prior to reporting of all trial details it is impossible to be sure of this. It should be remembered that in the Simplicity trials, however, office BP measurement was with an Omron device providing automatic paper printout, to protect against observer bias. Further, in the subsets of patients studied with 24-hour ambulatory blood pressure monitoring in the Simplicity HTN-1 and Simplicity HTN-2 trials, and in a much larger published ambulatory BP data base (Mahfoud et al, *Circulation* 2013;128:132-140), mean 24-hour systolic BP fall at the 6-month time point was 10-11 mm Hg. Ambulatory BP measurement protects against observer bias and placebo effect.

“The lady doth protest too much, methinks” (Queen Gertrude, Hamlet)? Not in this case, I believe (and I ask you to please forgive the gender confusion). I would wish the reader to be mindful of methods of decision-making in medical science and clinical medicine. In the past, medical knowledge derived from many sources. The historical starting point was often astute observation and description by doctors of the illness of their individual patients. This was elaborated on with autopsies (in the regrettable instances of medical failure), observations community-wide to detect patterns of the identified illness and its causes (epidemiology in its various forms), clinical investigation to better understand the biological mechanisms of disease (the “pathophysiology”), animal experimentation to confirm and extend these ideas, prevention and treatment strategies based on a logic deriving from all of the above, and observations in patients of the benefits, or lack of, when the logically-based treatments were applied. Some elements of this evidence path are strongly evident in the renal denervation saga.

Some emphases in “evidence-based medicine”, those which are too rigid and codified, have short-changed these ways of knowing, especially in relation to medical therapies. The final, and usually only, arbiter is the randomized double-blinded clinical trial, the other forms of medical knowledge not qualifying as real, or certainly not valuable evidence. My departing point is that although in therapeutics well designed clinical trials are of critical relevance, there are many ways of “knowing” in medicine. A single well-designed clinical trial can be fallible, as Simplicity HTN-3 could be, and should not stand alone as an absolute arbiter. The animal experimentation, the neural hypertension pathophysiology, and earlier clinical trials should not be forgotten.

## Read an interview with this month's New Investigator of the Month: Panagiotis Xaplanteris

Post-doctoral research fellow at Peripheral Vessels Unit, Hippokraton Hospital, 1st Department of Cardiology, Athens University Medical School, Athens, Greece

<http://ish-world.com/new-investigators-spotlight/i/April-spotlight-of-the-month/>





JOINT MEETING ESH-ISH  
**HYPERTENSION**  
ATHENS 2014

JUNE 13 - 16, 2014 - ATHENS, GREECE  
Megaron Athens International Conference Centre



24<sup>th</sup> European Meeting on Hypertension  
and Cardiovascular Protection



25<sup>th</sup> Scientific Meeting of the  
International Society of Hypertension

IN COOPERATION WITH



Asklepieion General  
Hospital Athens

Dear Friends, Dear Colleagues,

I have the pleasure in warmly inviting you to the forthcoming Joint Meeting of the European Society of Hypertension (ESH) and International Society of Hypertension (ISH), in collaboration with the Hellenic Society of Hypertension and the Cardiology Department of Asklepeion Hospital, which will be held in Athens, Greece, June 13-16, 2014.



The meeting will cover a large area of knowledge in the field not only of hypertension, but also other conditions related to hypertension such as: Dyslipidemias, diabetes mellitus, obesity, obstructive sleep apnea, coronary heart disease, heart failure, atrial fibrillation and new antithrombotics, peripheral arterial disease, COPD, sexual dysfunction etc.



As you know, the European and International Society of Hypertension meetings are the largest scientific events in hypertension worldwide, as they usually gather a huge number of participants all majorly or exclusively involved in hypertension and cardiovascular prevention at different levels. Delegates come from all over the world, and most worldwide authorities in the field of high blood pressure and related diseases are involved. This makes this event the most appropriate forum for reporting and discussing all emerging important diagnostic and therapeutic approaches with experts from all around the world.

The congress received more than 2,100 abstracts from 87 countries by the initial deadline (the highest number of abstracts ever received) and we still expect to receive additional abstracts by the "late breakers" deadline.

This important event will be held in Greece, the country of Asclepius and Hippocrates, who in their teachings "Το προλαμβάνειν προτιμότερον του θεραπεύειν εστί - prevention is preferable to curing (Hippokrates 460-377 B.C.)" and thus still today, these words are as current as ever in global medical thinking.

Athens, the cradle of classical thought, world culture, science and democracy is ready to welcome you and give you not only the ability to exchange views and information with experts from around the world, but also the opportunity to experience Greek history and hospitality.



We are expecting all of you on 13 to 16 June in Athens, do not miss the opportunity to meet experts in your field from around the world.

*Our motto is "we will all be there".*



Athanasios J. Manolis  
Chairman of the Organizing Committee

# New Investigator Committee (NIC) Update

The ISH New Investigator Committee Programme has now been finalized for the Hypertension Athens (Joint ESH-ISH) Meeting (June 13-16, 2014).

The Committee is happy to announce a series of oral and poster presentation award sessions to be included within the main meeting programme.



Dylan Burger, NIC Member

## 1. ISH NIC Oral Presentation session (June 14<sup>th</sup>- 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 15<sup>th</sup>- 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 14<sup>th</sup> 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

- A networking event for participants in the New Investigator Programme will follow the Welcome Reception on Friday June 13<sup>th</sup>. This will be a social event which will provide new investigators an opportunity to meet and interact with other new investigators as well as field leaders. This event will also feature the debut of the new ISH New Investigator Committee Logo and the launch of the new ISH Mentorship Scheme. For more information be sure to follow our updates on Facebook ([www.facebook.com/ISHNIN](http://www.facebook.com/ISHNIN)) and Twitter ([www.twitter.com/ISHNIN](http://www.twitter.com/ISHNIN)).

## 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.

**CALL FOR 2014 AWARD NOMINATIONS:  
DEADLINE 30<sup>TH</sup> APRIL**

**Please send the Secretariat your nominations for members to receive the following awards for 2014.**

- ISH Franz Volhard Award and Lectureship for Outstanding Research
- ISH Robert Tigerstedt Lifetime Achievement Award
- AstraZeneca Award
- ISH Developing World Award
- ISH Paul Korner Award, supported by the High Blood Pressure Research Foundation
- ISH Distinguished and Honorary Membership Awards



For detailed information please view the ISH website:

[http://ish-world.com/data/uploads/2014\\_awards\\_and\\_prizes\\_-\\_overview\\_for\\_website\\_updated\\_13\\_March\\_2014\\_2.pdf](http://ish-world.com/data/uploads/2014_awards_and_prizes_-_overview_for_website_updated_13_March_2014_2.pdf)

## The International Society of Hypertension partners with the World Hypertension League in advocating reduction of sodium intake to reduce cardiovascular disease



By Ernesto L. Schiffrin MD, PhD, President, ISH

The World Hypertension League (WHL), affiliated to the ISH, has its own board of directors and newsletter.

The WHL carries out mostly advocacy activities in contrast to the ISH that is a professional and scientific society. The President and the Past President of ISH sit on the WHL Board of Directors. The WHL acts quite independently of ISH. However, over the past year, the President of ISH and the new President of WHL (Dr. N.R.C. Campbell) have attempted to join in their efforts in order to strengthen the impact of some activities. Among these has been the compilation of a Hypertension Fact Sheet (which can be found on the ISH website [click here](#)) and a [joint policy Statement on Salt](#). The latter was the result of discussions in depth by members of WHL and the Executive of ISH. The Statement appeared in the February issue of Journal of Hypertension as ISH News: "The International Society of Hypertension and World Hypertension League call on governments, nongovernmental organizations and the food industry to work to reduce dietary sodium" (vol. 32, pp. 446-447). It also appeared simultaneously in the February issue of the Journal of Clinical Hypertension.

The policy expressly supported the World Health Organization and the United Nations recommendations on reduction of salt intake, which are based on a thorough review of research on the effects of excess salt on cardiovascular disease. The policy statement is a call for societal action to reduce excess dietary salt, in order to reduce blood pressure and prevent associated burden of cardiovascular disease. It is a call to hypertension organizations and experts to become more engaged in efforts to advocate to have dietary salt reduction policies endorsed by national hypertension organizations and international nongovernmental health organizations, particularly those member organizations of the ISH and the WHL. This will help in bringing about action from governments to implement excess salt intake reduction policies.

## WORLD HYPERTENSION DAY: 17 MAY

World Hypertension Day (WHD) was first inaugurated in May 2005 by the World Hypertension League (WHL) and has become an annual event ever since. The purpose of 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.

The theme for 2014 is **Know Your Blood Pressure**.

# WORLD HYPERTENSION DAY

*Initiated by the World Hypertension League*



Please see [www.worldhypertensionleague.org](http://www.worldhypertensionleague.org) for further information and to participate in the WHL's **global hypertension awareness survey**.

During the first two weeks of May 2014, WHL will do an analysis of how many people from each country participated in this survey and how many are in each of the categories (normal, potential hypertensives or pre-hypertensives and definite hypertensives). A report will then be issued by WHL on a country by country basis on 17<sup>th</sup> May.



## ANNA DOMINICZAK

Regius Professor of Medicine, Vice Principal & Head of The College of Medical, Veterinary and Life Sciences, University of Glasgow

President of the European Society of Hypertension

## The University of Glasgow College of Medical, Veterinary and Life Sciences was established in August 2010

Productive and collaborative, inter-disciplinary environments are required to solve the global challenges in biomedical science and population health. In recognition of this, the University of Glasgow underwent major restructuring in August 2010 with the amalgamation of three biomedical Faculties to form the College of Medical, Veterinary and Life Sciences (MVLS). The largest of the four Colleges in our University, MVLS now boasts a staff of 2000 and an annual turnover of £200 million per year.



### College of Medical, Veterinary and Life Sciences

#### 3 SCHOOLS

- School of Life Sciences
- School of Veterinary Medicine
- School of Medicine (including Dentistry and Nursing)

#### 7 INSTITUTES

- Cancer Sciences
- Cardiovascular & Medical Sciences
- Biodiversity, Animal Health & Comparative Medicine
- Infection, Immunity & Inflammation
- Molecular, Cell and Systems Biology
- Neuroscience and Psychology
- Institute of Health and Wellbeing

*Transformational change*



All the above are open for multidisciplinary and industrial collaborations

The College of MVLS comprises seven research institutes and three schools bringing together basic scientists and clinicians who work in partnership both across this structure and with other Colleges in the University of Glasgow (College of Engineering and College of Social Sciences). As a result we are able to study processes at every level of biological organisation, from genes, to cells, organs, individuals, populations and ecosystems. The College of MVLS is therefore uniquely placed to translate basic science into novel clinical applications and treatments which aim to tackle the major global health and wellbeing challenges of the 21<sup>st</sup> century.

### The Institute of Cardiovascular and Medical Sciences (ICAMS)

The Institute of Cardiovascular and Medical Science (ICAMS) is one of the College's seven multi-disciplinary research institutes, encompassing basic biomedical scientists, medical and veterinary clinicians and statisticians. The Institute holds the highly prestigious British Heart Foundation Research Excellence Centre, one of only six such centres in the UK.

Historically, the pioneering work was started by Drs Tony Lever, Jehoyda Brown and Ian Robertson in the 1960s who established the MRC Blood Pressure Unit. This set the stage early on for Glasgow as an internationally renowned hub of excellence in hypertension and cardiovascular science. In the 1980's, Professor John Reid developed international

excellence in clinical pharmacology and therapeutics, first as a Professor of Materia Medica and then as a Regius Professor of Medicine and Therapeutics (1989 - 2010) at the University of Glasgow.

Glasgow also boasted the first ever primary prevention trial with statins, the WOSCOPS study (Professors Jim Shepherd, Ian Ford, Chris Packard and Stuart Cobbe) as well as leading edge clinical work on heart failure (Professors John McMurray and Henry Dargie).

In 1997, the British Heart Foundation (BHF) funded a new BHF Chair and Programme on genetics of hypertension to Professor Anna Dominiczak. This was followed in 1999 by a major infrastructure award, also from the BHF, which allowed us to start a fundraising campaign run jointly by the University of Glasgow and the BHF to build a £20 million BHF Glasgow Cardiovascular Research Centre, which opened its doors in 2006 for the entire spectrum of cardiovascular research excellence in Glasgow, from bench to bedside and the population. Professor Anna Dominiczak became the founding Director of the Centre, the post she held until 2010.

## BHF Glasgow Cardiovascular Research Centre



The year 2010 brought the biggest revolution of academic life at the University since its birth in 1451. This resulted in major gains for cardiovascular research, which by that stage was firmly established as one of the major research priorities at the University and the new College.

We were very fortunate to recruit from Canada, Professor Rhian Touyz, an internationally renowned clinician scientist, to become the first Director of the Institute of Cardiovascular and Medical Sciences (ICAMS) in 2011. As all readers of this Newsletter know, Professor Touyz is the President Elect of ISH.

The mission of the Institute is to enhance human health through research into the fundamental mechanisms of cardiovascular disease and the discovery of novel therapeutics to advance diagnosis and treatment.



### RHIAN TOUYZ

BHF Professor of Cardiovascular Medicine, Director of the Institute of Cardiovascular and Medical Sciences, University of Glasgow



### ANDREW BAKER

BHF Professor of Translational Cardiovascular Sciences, Deputy Director of the Institute of Cardiovascular and Medical Sciences, University of Glasgow



## Institute of Cardiovascular and Medical Sciences

Vision: To be a world leader bridging the gap between cardiovascular science and medicine through excellent research & teaching

### Who we are

- Research-intensive institute focusing on cardiovascular science
- 192 staff; >130 students; 36 professors; Clinical and non-clinical
- Annual budget ~£30M

### Our strategic research priorities

- Vascular Pathophysiology & Therapy
- Heart Research
- Diabetes, Renal, Endocrinology & Metabolic Disease
- Genetics, Genomics & Systems Medicine
- Clinical Trials & Implementation

### Our recent successes

- BHF Centre of Excellence
- BHF Regenerative Medicine Awards (Vascular; Cardiac)
- 2 BHF Chairs
- 2 Spin out companies

### Our funding sources



### Our Research



The Institute's research portfolio is aligned into five key research themes, each with an internationally recognised profile. There are now more than 200 ICAMS staff members.

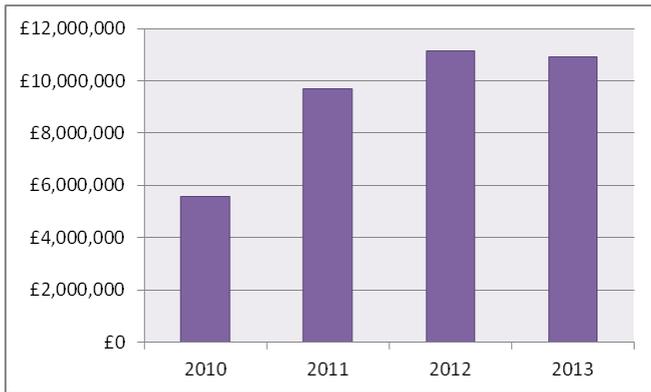
## ICAMS peer reviewed funding 2010-2013

Research in ICAMS results in over 350 publications per year, many within the top ranking journals, and attracts substantial external research grant income. Major grants include support for the first-in-man trial of gene therapy (Medical Research Council and British Heart Foundation), the identification of biomarkers for chronic disease (Scottish Funding Council and European Commission) and vascular therapeutic targets and regenerative strategies (British Heart Foundation).

# Join us in Athens in June!



**Peer-reviewed funding since formation of ICAMS in 2010 to 2013:**



**Educational opportunities**

Integral to the Institute’s core mission is its commitment to nurture and inspire the next generation of clinical and non-clinical scientists through an outstanding training programme. There are over 120 students, 40% of whom are from overseas. A broad range of undergraduate and graduate training opportunities are offered across the diverse range of Institute research strengths, all within a well-connected clinical environment.

**Bench-to-bedside ethos**

A major focus of ICAMS, and indeed the wider College’s work is the translation of mechanistic science into advances in clinical practice and therapeutics to prevent, diagnose and treat cardiovascular disease. Supporting this mission is the Glasgow Biomedicine Board - a partnership between the University of Glasgow and the National Health Service (NHS) that facilitates and streamlines the conduct of multi-centre international randomised controlled clinical trials. Scotland’s centralised health records with unique patient identifiers enable accurate analysis of trial data and patient follow-up to establish crucial long-term clinical outcomes. Furthermore, the high prevalence of cardiovascular disease and related co-morbidities in the West of Scotland provides access to a large pool of patients from the local population ensuring effective recruitment to these trials. Our researchers have led or played major roles in some of the most ground-breaking and practice changing cardiovascular studies of the last two decades and our world class reputation has invited involvement of our staff in clinical guideline development at the highest level.

Flagship studies involving the Institute of Cardiovascular and Medical Sciences	
WOSCOPS	West of Scotland Coronary Prevention Study - <i>N Engl J Med.</i> 1995; 333: 1301-1307 & <i>N Engl J Med.</i> 2007; 357: 1477-1486
PROSPER	PROspective Study of Pravastatin in the Elderly at Risk - <i>Lancet</i> 2002; 360: 1623-1630

CIBIS-2	The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial - <i>Lancet</i> 1999; 353: 9-13.
BRIGHT	Genome-wide mapping of human loci for essential hypertension - <i>Lancet</i> 2003;361:2118-23  Linkage analysis using co-phenotypes in the BRIGHT study reveals novel potential susceptibility loci for hypertension - <i>Am J Hum Genet</i> 2006;79:323-31  Gene-centric association signals for lipids and apolipoproteins identified via the HumanCVD BeadChip - <i>Am J Hum Genet</i> 2009;85:628-42  British Genetics of Hypertension Study - <i>Hypertension</i> 2006;47: 603-8
EMPHASIS-HF	Eplerenone in patients with systolic heart failure and mild symptoms - <i>N Engl J Med</i> 2011; 364:11-21
CHARM	Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial - <i>Lancet</i> 2003; 362: 767-771  Relationship of dose of background angiotensin-converting enzyme inhibitor to the benefits of candesartan in the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM)-Added trial - <i>Am Heart J</i> 2006; 151: 985-991  Resource utilization and costs in the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) programme - <i>Eur Heart J</i> 2006; 27: 1447-1458
NAVIGATOR	Effect of valsartan on the incidence of diabetes and cardiovascular events - <i>N Engl J Med</i> 2010; 362: 1477-1490  Effect of nateglinide on the incidence of diabetes and cardiovascular events - <i>N Engl J Med</i> 2010; 362: 1463-1476
CORONA	Rosuvastatin in older patients with systolic heart failure - <i>N Engl J Med.</i>

2007 Nov 29;357(22):2248-61

Effects of statin therapy according to plasma high-sensitivity C-reactive protein concentration in the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA): a retrospective analysis - *Circulation*. 2009 Dec 1;120(22):2188-96

### Stratified Medicine Scotland Innovation Centre

With the era of stratified medicine upon us, the University of Glasgow is leading the creation of a Stratified Medicine Scotland Innovation Centre (SMS-IC). This ambitious venture, due to complete in mid-2015, brings together the NHS and industry along with the Universities of Aberdeen, Dundee and Edinburgh and will be located at the new South Glasgow Hospitals Campus, one of the largest academic hospitals in Europe. The SMS-IC will place Glasgow at the forefront of genomic medicine promoting research into the genetic basis of disease and the development of optimised therapies based on patient's individual genetic make-up. This work will progress to stratified clinical trials to determine the efficacy of this treatment approach. The benefits of stratified medicine include limitation of futile prescribing thereby reducing adverse treatment effects and improving cost-effectiveness. The approach is anticipated to apply to a range of chronic conditions such as cancer, cardiovascular disease, rheumatoid arthritis and respiratory disease that burden our population and health services. Collectively, the SMS-IC will further strengthen our College's close links with the NHS and uniquely position the University of Glasgow to revolutionise the way we prescribe medications to treat chronic disease.

### Stratified Medicine Scotland Innovation Centre



## ODD CORNER FROM THE LANCET

### IS FOOTBALL DANGEROUS ?

THE death of Sydney Branson, a promising student of St. George's Hospital, from injuries received during a football match, has provoked a discussion in the daily press as to the dangers attendant on that game. In answering the question, "Is football dangerous?" we would distinguish between the game as played by boys and as played by men. With respect to boys, we believe the game, even the much-abused Rugby game, to be as safe as any other athletic pursuit, provided always that the boys engaged in it are sound and healthy.

With grown-up men the case is different. Football is essentially a rough-and-tumble game, and a man does not fall as lightly or as cleverly as a boy can; a collision which simply "knocks the wind out" of the latter may seriously injure or even rupture some important organ in the former. But the case is more dangerous still to young men engaged in sedentary occupations all the week, and who get a chance game on Saturday only; in their case the muscles are relaxed, and consequently they have less perfect control over their movements, and therefore are less able to keep out of danger and avoid collisions by those instinctive muscular actions which would save a man whose muscles were in perfect tone. The intense strain that a football match requires must act most injuriously upon an untrained man; it is not uncommon at a football match to see men, of the class we are describing, become faint and vomit after a charge or "scrimmage." We would not discourage any manly sport, but we would insist that in every case the physical exertion should be adapted to the age, strength, and habits of the individual.

THE LANCET,]

[APRIL 3, 1875.

## REGIONAL ACTIVITIES & REPORTS

### CENTRAL AND SOUTH AMERICA

The XI Latin American Congress on Hypertension was held from 8-11 October 2013, in Margarita Island, Venezuela; organized by the Latin American Society of Hypertension and Venezuelan Society of Hypertension, with the important support of the European Society of Hypertension, International Society of Hypertension, Department of Hypertension of the Brazilian Society of Cardiology and the Brazilian Society of Hypertension.

About 1,000 doctors from Argentina, Brazil, Colombia, Ecuador, Peru, Mexico and Venezuela attended the three day meeting. Fifty professors participated as faculty members including Professors Alberto Zanchetti, Giuseppe Mancia, Josep Redon, Antonio Coca, Ramiro Sánchez, Patricio López-Jaramillo, Eduardo Barbosa and Rafael Hernández-Hernández who attended the first day. This was devoted to the European Society of Hypertension (ESH)/Latin American Society of Hypertension (LASH) Master Course.



The new ESH/ESC hypertension guidelines and the Latin American Hypertension Guidelines were discussed in detail and state of the art sessions were held on resistant hypertension diagnosis and new ways of treatment, new developments of the renin-angiotensin system; new way of handling hypertension management; endothelium and hypertension, new insights on blood pressure monitoring and recording, amongst many other topics. The program was clinically orientated, but covering all the essential basic, epidemiological, and therapeutic aspects necessary for physicians and researchers.

Among the 80 free communications selected to be presented at the congress, two presenters received awards at the end of the meeting. Judges included Drs. Daniel Piskorz, Nora López and Jose Andrés Octavio, from Argentina and Venezuela.

LASH elected Professors Giuseppe Mancia and Josep Redon, as new Honorary Members of the Society, due to their outstanding contributions to medical research and their impact on medical education for Latin American doctors.

Physicians from Argentina, Brazil, and Venezuela received LASH Clinical Hypertension Specialist certificates, after completing the LASH Specialist Program which was established in 2002.

The congress was organised by:

**President:** Rafael Hernández Hernández  
**First Vice-President Executive and President of LASH:** Ramiro Sánchez  
**Second Vice-President:** Agustín Ramírez  
**Secretary:** Jesús López Rivera  
**Treasurer:** María José Armas

**Members**

- Eduardo Barbosa
- Weimar Sebba Barroso
- Patricio López Jaramillo
- Ernesto Peña Herrera
- Alfonso Bryce

**Free communications Committee**

- Igor Morr
- Luis Alcocer
- Daniel Piskorz
- José Andrés Octavio
- Nora López

**International support Committee**

- Alberto Zanchetti
- Antonio Coca
- Giuseppe Mancia
- Josep Redón
- Ernesto Schiffrin
- Stephen Harrap
- Maria Claudia Irigoyen
- Roberto da Silva Franco



**Agustin Ramirez MD, PhD**

## MEMBERSHIP INFORMATION

### ISH Secretariat New Contact Details

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

**ISH Secretariat**  
c/o The Conference Collective Ltd.  
Suite 2, Churcham House, 1 Bridgeman Road  
Teddington  
Middlesex, TW11 9AJ  
United Kingdom

*Tel (UK):* +44 (0) 20 8977 7997  
*Email:* [secretariat@ish-world.com](mailto:secretariat@ish-world.com)

*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 visit the membership section of [www.ish-world.com](http://www.ish-world.com). Alternatively, 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](http://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](mailto:secretariat@ish-world.com) with any questions.**

## ISH CORPORATE MEMBERS

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



Join us in Athens  
13-16 June 2014!

International Society of Hypertension Secretariat  
c/o The Conference Collective  
Email: [secretariat@ish-world.com](mailto:secretariat@ish-world.com) / Website: [www.ish-world.com](http://www.ish-world.com)

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