INTERNATIONAL SOCIETY OF HYPERTENSION

Hypertension News

Opus 12
29 March 2007

VOTE

on the New
ISH Constitution

36% of the ISH members have already done so

President's address
Lars H Lindholm, Sweden

First, sincere thanks to Lawrie Beilin for editing this issue of Hypertension News. Second, let me discuss two important ISH matters with you. The new ISH Constitution (former By-laws) and the revised list of ISH members.

The change of the ISH By-laws. As you know, we recently moved the ISH secretariat from Geneva to London. This turned out to be much better than expected. In London, the staff of Hampton Medical Conferences Ltd. look after us in an excellent way. However, the move from Geneva to London makes it necessary for the Society to get registered in the UK as a charity organisation. With the help of Hampton Medical and Wilsons' solicitors in London, the ISH By-laws have now been rewritten and are called "Constitution" and, some weeks ago, we e-mailed you a copy for your acceptance. The full ISH Council stand behind this new Constitution. The solicitor, who has worked for the Charity Commission herself, has given us the following comments on the final draft: "The draft Constitution which I have produced includes all of the provisions recommended by the Charity Commission and should ensure that the charity registration process for the Society is as smooth as possible." Almost all changes have been made for "fiscal" reasons (we want to avoid tax, VAT etc). However, we have also amended the writing about the Board of Management (BoM) of the Journal of Hypertension so it mirrors what we in fact do today. Both the old By-laws and the new Constitution can be found on the ISH web site (www.ish-world.com). We must now ask you to send us your vote on the new Constitution, unless you have already done so. A voting form is enclosed this issue of Hypertension News (Opus 12). Please send this by fax or mail to the number or address given on the form. Unfortunately, according to the old By-laws, we can not accept voting by e-mail. We must get a vote from more than half our members (!), with 2/3 affirmative, to get the new Constitution adopted. So far, around 249 members (36%) have voted.

The revised list of ISH members. The old ISH membership list was in great need of revision. Many members were either dead, retired since many years, or had left the cardiovascular research field altogether. Several had not paid their annual dues for many years. We have gone over the list several times and some of you have helped us contact members from your respective country. Our Secretary, Tony Heagerty, prepared a list of around 250 members who the Executive Committee decided to strike off the list in February 2007, according to the ISH By-laws Article III p. 7.1 (They had not paid their dues for 2005, 2006, and 2007). They will, however, be put back on the list of members, should they decide to pay for 2007. The Secretary has also prepared a list of 22 members suggested for "Emeritus status" which will be discussed by the Membership Committee in Milan in June. We also have a list of around 40 who have applied for ISH membership but who have not yet had this confirmed by the ISH General Meeting. The inflow of applications is good but we would be grateful if you helped us recruit more! The membership list will be published shortly on the ISH website (hidden pages). You can get your private code from Hampton, unless you already have it! At the Council meetings in Milan 2005 and in Fukuoka 2006, it was made clear that ISH should not have a two tiered membership scheme with different dues etc. However, "student membership" could be accepted to make membership more accessible for young investigators and to encourage wider participation in Society activities. This will be further discussed at the next Council meeting in June in Milan.

A form for new members is enclosed. (pp10-11)

Report on the 'ISH Teaching Seminar', organised by the 'ISH Low and Middle Income Countries Committee' in Maputo, Mozambique, on September 21-22 2006

R. Fagard, Belgium, on behalf of A. Damasceno, D. Lemogoum, J.R. M'Buyamba-Kabangu, S. Mendis, B. Onwubere, J. Polonia and Y. Seedat.

The main purpose of the 'Low and Middle Income Countries Committee' of the International Society of Hypertension is to encourage and enhance education and biomedical research in the fields of hypertension and associated cardiovascular diseases in the developing world. In agreement with this mission, the "Europe-Africa Subcommittee" organised its first "ISH Teaching Seminar" in Maputo, Mozambique, on September 21-22 2006, under the direction of R. Fagard and local host A. Damasceno, and in collaboration with the International Forum for Hypertension Control and Prevention in Africa (IFHA). Other faculty members were D. Lemogoum (Cameroun), J.R. M'Buyamba-Kabangu (D.R. Congo), S. Mendis (WHO), B. Onwubere (Nigeria), J. Polonia (Portugal) and Y. Seedat (South Africa).

A. Damasceno reported that, whereas hypertension was apparently almost absent in Sub-Saharan Africa (SSA) about a century ago, hypertension is now highly prevalent, mainly in urban areas. The urbanization process has created drastic changes in the previously healthy way of living characteristics in the rural African setting, including a sedentary lifestyle, increases in alcohol and tobacco consumption, more stress and changes in diet, resulting in obesity, diabetes and hypertension. As reviewed by B. Onwubere cardiovascular diseases (CVD) now account for nearly a quarter of all deaths in developing nations, and, in fact, 80% of CVD-related deaths in the world occur in developing countries. Stroke, heart failure and renal disease appear to be the commonest complications of hypertension in SSA. Unfortunately, more severe complications of hypertension contrast with low levels of awareness. The economic burden of hypertension is considerable and, in the poor socio-economic setting of SSA, prevention would be most desirable.

J. Polonia unravelled the pathophysiology of hypertension in blacks. It is of note, however, that most data have been obtained in African Americans and it is not certain that these findings apply to SSA, where, in addition, regional differences may exist. Environmental factors and socio-economic status probably play a major role, but other factors may be involved such as salt sensitivity, low plasma renin, low birth weight and genetic susceptibility.

Reliable blood pressure (BP) measurements are a prerequisite for diagnosis and management of hypertension. S. Mendis reviewed the requirements for reliable and affordable instrumentation in low resource settings and mentioned that at least one company has an interest in producing such a device at low cost. Although self-measurement of BP at home and ambulatory BP monitoring may currently have limited application in SSA, R. Fagard reviewed the value of out-of-office BP measurements and the concepts of white-coat, masked and sustained hypertension.

Y. Seedat stressed that the concept of risk stratification for the management of hypertension should also be applied in SSA, but modified according to the WHO CVD risk management package for low and medium resource settings. J.R. M'Buyamba-Kabangu reiterated the importance of the paradigm shift from focusing on single risk factors to comprehensive CV risk management and reviewed the highly recommended WHO CVD risk management package, meant to be implemented in a range of health care facilities in low- and medium resource settings,

depending on the available resources in terms of skilled personnel, diagnostic and therapeutic facilities and health services. S. Mendis emphasized that the benefits and cost-effectiveness of managing hypertension depend on the total CV risk and not on BP alone. Because individuals at low CV risk with mild hypertension account for a considerable share of the global CVD burden, all attempts must be made to address those at low risk using population-based upstream policies that promote healthy lifestyle. Risk assessment methods need to be developed to stratify total CV risk using simple variables such as age, sex, tobacco use, family history and presence or absence of hypertension and diabetes. Limited resources can then be used more effectively and efficiently for focusing drug treatment on those at high total CV risk, who are most likely to benefit.

D. Lemogoum confirmed the importance of lifestyle intervention offering a unique opportunity to reduce the burden of hypertension in SSA. Population-based strategies aimed at shifting the levels of risk factors to lower values in the entire population are likely to lead to a substantial reduction of the global CVD burden. Reduction in salt intake may be particularly useful in blacks, next to from weight loss, increased physical activity, reduced tobacco use, limited alcohol consumption, reduced intake of saturated fats and increased consumption of fruits and vegetables. A strong political commitment would, however, be necessary to achieve these goals.

With regard to the initiation of pharmacological antihypertensive therapy, B. Onwubere stressed that individualisation is the key point, taking cognizance of the individual's circumstances including CV risk, target organ damage and associated clinical conditions. This involves a compromise because, although benefit at the level of the individual rises as the treatment threshold increases, the benefit at the population level falls. Y. Seedat discussed the important issue of drug treatment of hypertension in SSA. Thiazide-like diuretics are the baseline antihypertensive agents. They are more effective than in whites, probably related to an expanded extracellular volume and low plasma renin activity, and their cost is low. Calcium channel blockers show the most consistent response in blacks compared with other classes of drugs as monotherapy. Beta-blockers and ACE-inhibitors appear to be hardly different from placebo. It is important to remember that there are no outcome data on morbidity and mortality in blacks in SSA. In addition, hypertensive crises are not uncommon in SSA and J. Polonia reported on the various manifestations and the most appropriate management.

Finally, A. Damasceno and R. Fagard commented on, respectively, "How to set up an epidemiological study" and "How to set up an intervention study".

The seminar was attended by 28 participants, 13 from Mozambique, 8 from Nigeria, 2 from Tanzania, and 1 from Angola, D.R. Congo, Mauritius, Ruanda and Uganda. Twelve of them presented their own research in SSA, based on a call for abstracts. These communications covered population epidemiology, BP control in different settings, target organ damage (left ventricular hypertrophy), incidence of stroke and prevalence of the metabolic syndrome. The abstracts strengthened the fact that hypertension and its complications are prevalent in SSA, but that awareness and BP control are poor.

The "ISH Teaching Seminar" was supported by the World Heart Federation, the World Health Organisation, the European Society of Hypertension, the Belgian Hypertension Committee and the University of Leuven (Belgium) and a number of corporate sponsors (Servier; Bayer; Boehringer-Ingelheim; Bristol-Myers-Squibb; Pfizer; Sanofi-Aventis; AstraZeneca; Novartis; Sankyo; Solvay; Therabel; Merck Sharp & Dohme).

In view of the success of the first seminar, ISH has decided to organise a second seminar for French speaking African countries in Douala, Cameroun, in March 2008, in collaboration with IFHA.

Hypertension research: Looking into the crystal ball.

Ernesto L. Schiffrin, Canada

As Yogi Berra famously taught us, “it is always difficult to predict, especially about the future.” Futurologists are often off the mark. Our predictions in fact often turn out in part to be the result of wishful thinking. They may be exaggerated or overly optimistic. On the contrary, sometimes we are unable to even remotely conceive the developments that will indeed take place, the quantum leaps that occur in knowledge and science at watershed points in our progress forward in time. Predictions are perhaps even more difficult in biomedicine than in other fields, since breakthroughs often occur serendipitously in small, obscure laboratories away from the limelight and far from the mainstream, where an investigator carries out research that initially gets little notice and may even generate marked skepticism within the scientific community until evidence of the biological advance in our knowledge that the particular research signifies becomes overwhelming and convincing. With this caveat in place, it is easier to let the imagination run loose, and think of what lies ahead in cardiovascular research, more specifically for hypertension, in the next few years.

Developments will occur in the identification of new molecules that play roles in hypertension. With our ability to use yeast two hybrids and the availability of libraries and methodologies that allow molecules involved in protein-protein interactions to be demonstrated, regulatory factors modulating enzymes and other proteins, novel signaling molecules and transcription factors will be discovered, and the regulation of cellular processes that carry out major cell functions delineated to much greater extent than we know today, and their complexity better understood. This will allow on the one hand gaining greater insight into the human genome and proteome, and their functioning, identification of the huge numbers of genes and gene products that remain to be identified, and pinpointing on the basis of molecular and genetic research mechanisms and pathways involved in cardiovascular dysfunction. Examples are the explosive developments in our knowledge of how vascular smooth muscle cells or cardiac cells (cardiomyocytes and fibroblasts) differentially generate in a cell- and species-specific way, reactive oxygen species that play a critical physiological role in signal transduction, and as well a pathophysiological role in oxidative damage. Specific regulatory molecules such as Nox 1, 2, 4, 5, and possibly even Duox1/2 involved in generation of reactive oxygen species will be further identified and characterized. Development of agents that may interfere with the normal functioning of some of these regulatory molecules may represent potential additions to our therapeutic armamentarium for the treatment of cardiovascular disease. Similarly, the identification of mutations and polymorphisms that provide opportunities for diagnosis and eventually for genetic interventions will continue at an increasingly rapid rate. Another example is the explosive knowledge regarding mechanisms whereby renal disease accelerates cardiovascular disease. Findings include the identification of numerous mechanisms and agents such as fetuin-A, matrix Gla protein (MGP), osteoprotegerin, bone morphogenetic proteins (BMPs), the role of pyrophosphate and others, which regulate calcification of vessels and create opportunities for therapeutic intervention.

On a clinical basis, full genome scans and progress in linking specific genes with subsets of hypertension and other cardiovascular conditions will help clarify the genetic basis of high blood pressure in humans and identify at the same time new mechanisms contributing to cardiovascular risk. With our realization that total cardiovascular risk needs to be addressed in our patients, it would be very useful to be able to use a simple biomarker to identify people at high cardiovascular risk. There is growing interest in identifying such a marker that could be cheaply and easily measured and become available in primary care facilities.

I am persuaded that our ability to identify individuals at high risk, and to adequately stratify cardiovascular risk at different levels of blood pressure, will increase. We will also use non invasive techniques to assess the state of the vasculature, and thus provide a more complete evaluation added to blood pressure measurements. Blood pressure measurement will remain nevertheless the main method for clinical evaluation and risk assessment in hypertension, albeit with instrumentation that will be refined relative to currently available equipment. Automatic devices that average repeated measures taken over short periods of time, some already available, and greater use of self-measurement of blood pressure, will themselves allow more precise and reliable blood pressure measurement with less interference of an alert reaction and clinic-induced hypertensive responses. Many of these will increasingly be used and go from the phase of evaluation in clinical research situations to generalized clinical use, however slowly this transfer process may occur. The use of circulating biomarkers to evaluate risk will also become more generalized as epidemiologic studies provide evidence of the value of specific markers, over and above more traditional measures including blood pressure or measures of vascular stiffness and function, allowing us to have greater certitude about who has to be treated more aggressively. Progress in imaging techniques may be so phenomenal as to be totally and completely unpredictable, and could also allow us to non invasively evaluate fluid dynamic changes that may represent increased risk, generating as well opportunities to correct vascular abnormalities with minimally invasive surgical approaches.

Progress will without doubt occur with identification of new therapies based on new agents resulting from rational drug design using modeling techniques and identification of new targets based on molecular and cellular research, as well as development of biological agents with specific properties. There will be refinement in currently available agents, and improved bioavailability and reduced adverse effects of some of the more interesting drugs that are already available for human therapeutics. New delivery modalities may permit the simultaneous administration of multiple medications in single pills or capsules, in which the properties of the components will allow differential rates of delivery for each of the molecules, a variation on the concept of combination therapy or even the “polypill”. Circadian variations in the rate of administration of agents using slow delivery and extra long acting agents will allow medications to be delivered in the most adequate and pharmacologically appropriate way with administration once a week or even once a month for many drugs, which will reduce the lack of compliance with drug therapy that plagues treatment of many chronic diseases. Significant progress in pharmacogenomics will allow treatment to be individualized to a much greater extent than is possible today, avoiding the unnecessary use of certain agents in individuals who will either not respond optimally to them, or who may develop adverse side-effects with defined agents that can thus be identified in advance. However, apart from the discovery of new pathways, new agents, new diagnostic techniques for early detection and refinement of risk stratification, hopefully we will make progress in our ability to deliver health-care across the world, in developed and in middle- and low-income countries, with cheaper and more efficient models of health-care delivery.

More effective knowledge transfer, taking advantage of the huge progress and the reduced cost of the newer means of communication and the Internet, the increased wider application of telemedicine, greater access to care, cheaper medications, will all hopefully contribute together with molecular, cellular, pharmacologic and diagnostic progress to improve outcomes and reduce the burden of disease caused by hypertension. What exciting times lie ahead of us in hypertension research!

Nobel Ambitions in Hypertension
Stephen Harrap , Australia

Is there a Nobel Prize awaiting researchers in hypertension? I'm not sure whether this question plays on the minds of many of us in the blood pressure world, but simply as an academic exercise, it's worth a thought.

To address this question we need to look at the possibilities. The first issue is the number of Prizes awarded each year. These days there are 6 Prizes awarded annually in Physics, Chemistry, Physiology or Medicine, Literature, Peace and Economics.

Other than Physiology or Medicine, it's hard to image hypertension finding its way to the top in the other categories. Although, achieving a denouement in the salt and blood pressure debate might merit the Peace Prize!

The trick is to know what the Physiology or Medicine Committee is looking for. One can get an idea by looking back over the Prizes since the first was awarded in 1901. As it happens the very first (to von Behring) was awarded for diphtheria and it seems that research involving infection or immunity is highly regarded by the Committee. In all 26 Prizes have fallen under this category, the most recent being that for Helicobacter and gastric ulcers in 2005 (Marshall and Warren).

Although there has been some work on infectious issues in relation to coronary disease, a quick search of Medline under the combination of infection and hypertension brings up portal and pulmonary hypertension, but very little on the topic of systemic hypertension. Simply on critical mass, this approach doesn't look like a winner for hypertension.

Of course it could be claimed that hypertension has already won some Nobel Prizes. In 1998 Furchgott, Ignarro and Murad won their prize for discoveries concerning nitric oxide as a signaling molecule in the cardiovascular system. The discovery by Sir James Black of beta-adrenergic blockers drugs for which he won the Prize in 1988 with Elion and Hitchings was also highly relevant to hypertension. One might also make a case for the 1982 Prize for discoveries concerning prostaglandins (Bergström, Samuelsson & Vane) and possibly even stretch to the 1956 the Prize (Cournand, Forssmann and Dickinson) for discoveries concerning heart catheterization and pathological changes in the circulatory system.

However, this sort of reflected glory emphasizes a problem for hypertension. The joy of regular hypertension conferences is the diversity of research issues presented and discussed. Yet it is the multifactorial and complex nature of hypertension that makes it a rather amorphous target for the Nobel Committee to consider.

It is clear from the trends in Prizes over recent decades that Nobel Prizes favor the reductionist rather than the integrative discoveries. This is especially evident in the molecular realms. Take for example the most recent Prize for the discovery of RNA interference (Fire and Mello, 2006) or the 2004 Prize for odorant receptors (Axel & Buck), apoptosis in 2002 (Brenner, Horvitz and Sulston), G-proteins in 1994 (Gilman & Rodbell), split genes in 1993 (Roberts and Sharp), single ion channels in 1991 (Neher & Sakmann) and so on.

Assuming this trend continues, what are the chances for hypertension? My guess is that if it eventuates it will come, as do the best discoveries, as serendipity or what the military might call a collateral discovery. There's a fair chance that in chasing down something under the umbrella of hypertension, a discovery with wide-ranging ramifications will be made.

This might come as the discovery of new genes or genetic control mechanisms that unlock pathways of biochemical and physiological control previously unimagined.

The final question then is does hypertension research have an edge over other fields in terms of such discoveries. We find ourselves using similar methodological approaches as those studying obesity, diabetes, asthma, arthritis and so forth. Obviously luck and hard work will come into the equation, but the continuation of hypertension as an integrated research community heightens the potential to translate rapidly and strategically from molecular discovery to clinical relevance.

If nothing else, the preservation of our regular meetings that cross-pollinate the broad range of disciplines under the hypertension barrier is essential. Who knows, in the future you might get to rub shoulders regularly with a Nobel Laureate at ISH Scientific Meetings!

ESH/ISH JOINT SCIENTIFIC MEETING 2014

The Councils of the European Society of Hypertension (ESH) and the International Society of Hypertension (ISH) have agreed to hold a Joint Scientific Meeting in Europe in 2014. Both Councils would welcome bids from scientists, research groups or European National Societies of Hypertension to host this meeting.

Previous conferences have attracted more than 5,000 delegates and local organisers should be prepared to host a meeting of at least this size and to meet with the terms set by the two Societies.

Prospective applicants should prepare a comprehensive proposal to be submitted to the ESH/ISH 2014 Secretariat by 15 May, 2007. Please contact Mrs Jacinta Scannell at the Secretariat to receive a copy of the full bid requirements. Contact details are shown below.

A final decision will be made by representatives of both Councils at the forthcoming ESH meeting in Milan on 17 June 2007. Applicants may present further printed material at this meeting and also make a short (10 minute) presentation of their respective bid.

Contact:
Mrs Jacinta Scannell
ESH/ISH 2014 Secretariat
c/o Hampton Medical Conferences
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TW12 1NJ
Tel: +44 (0) 20 8979 8300
Email: secretariat@ish-world.com

Membership

If you have not yet renewed your ISH membership for 2006 now is the time to do so to ensure you continue to receive copies of the Journal of Hypertension and subsequent copies of the Newsletter.

Payment can be made **on-line by visiting www.ish-world.com** Note: **You will be required to quote your membership number** (if you do not know this, it can be obtained be emailing secretariat@ish-world.com).
Go to the Membership page and click on Membership Fees. A confirmation email will be sent to you.

Newsletter

Within the next month or so there will also be a members' only area on the new ISH website (www.ish-world.com) where members will be able to read past copies of the ISH Newsletter.

In addition, HMC maintain the electronic ISH membership database and keep it updated with address changes, etc. If you have not already done so, please complete and fax back the form below.

Recruit New Members

We would welcome your assistance to help us recruit new members to the Society. The Society welcomes applications for membership from individuals working in the field of hypertension and cardiovascular disease.
If you have a colleague who would like to become a member of the International Society of Hypertension, please ask them to complete the downloadable Application Form that can be found on the Society's new website: **www.ish-world.com**. Applications must also be accompanied by:

1. A written statement by two members of the Society (names of regional/national members can be provided by the Secretariat) as to the qualifications of the nominee;
2. A list of the nominee's academic degrees, professional positions, and a list of five best and five most recent publications relating to hypertension or allied fields.

Nominations are initially considered by the Membership Committee and ultimately approved by the Society at its biennial scientific meetings.
If you have any questions regarding your membership, please do not hesitate to contact us.

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PLEASE FILL IN AND RETURN TO THE ISH SECRETARIAT AT THE ADDRESS BELOW

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