ESC congress news

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BARCELONA 2014

Adapting to a changing environment in research, education and technology

WITH MEDICINE at a cross-roads for 'critical change', ESC President Professor Panos Vardas said it was 'imperative' for the Society to adapt to fast evolving modern environments.

'The leaderships of our Associations must acknowledge developments in those strategic areas likely to influence our prospects,' Professor Vardas told a packed Inaugural Session yesterday. Quoting the Greek philosopher Philostratus, he warned: 'Wise men perceive approaching things.'

Sharing his own perspective on such 'approaching things', Professor Vardas predicted that understanding the digital health revolution would prove crucial. 'The ESC should seek to establish channels of communication with the large digital technology players who offer the potential to provide new streams of revenue,' said Professor Vardas, who steps down as ESC President on Tuesday.

Postgraduate education and professional development, areas once dominated by universities and scientific societies, have been targeted recently by for-profit organisations operating over the internet. 'Faced with these evolving realities, medical associations should collaborate with selected academic institutes,' said Professor Vardas.

He announced that the European Heart Academy, one of the three new ESC satellite institutes in Brussels, will collaborate with the London School of Economics to develop a two-year course in Health Economics, Outcomes and Management in Cardiovascular Sciences leading to a Master's degree.

The standing of academic medicine has suffered setbacks in recent years, with remuneration of academics falling behind that of clinicians. 'It's important to promote our values and persuade policy makers of the need to make academic medicine the attractive career choice it used to be,' said Professor Vardas.

Outgoing ESC President Panos Vardas: Imperative that the ESC adapts to fast evolving modern environments. 'Wise men perceive approaching things,' he warned.

On healthcare systems, Professor Vardas warned that heterogeneity leads to inequalities. The ESC, he said, was not only creating guidelines but developing initiatives, such as the Atlas of Cardiovascular Health Care Systems, to address such inequalities.

He noted that the demystification of healthcare information is catalysing the move for patients to become partners in their treatment. 'It seems that consumers will dominate healthcare and any healthcare institution ignoring this trend does so at its peril,' said Professor Vardas.

While medical innovations have extended the life expectancy of cardiovascular patients by eight to ten years, the field has become a 'victim of its own success'. As a result of patent loss, Professor Vardas explained, the compound annual growth rate in pharmaceutical companies currently stands at -10%. 'Such decline can prove disastrous for research and jeopardise the future of our medical associations, which largely depend on industry support,' he said. 'We need to go to the next level of innovation, in stems cells, tissue engineering and nanotechnology.'

By placing its spotlight on innovation, ESC Congress 2014 hopes to further stimulate research in cardiovascular science. Professor Vardas paid tribute to this year's ESC Gold Medallists Sir Rory Collins, Petr Widimsky and Alain Carpentier. 'Their innovations in population studies, acute cardiac care and valve surgery have truly changed the way we practise cardiology,' he said.

Also speaking of ESC Congress 2014, Professor Keith Fox, Chairperson of the Congress Programme Committee, highlighted innovations in the way the programme will be delivered this year. These include moderated e-posters and a mobile phone app which allows delegates to put their questions directly to panellists in the global focus sessions.

The first certificate of excellence in training in interventional cardiology was also awarded to Professor Marc Hartmann from Thorax Centrum Twente in Enschede, the Netherlands. The training programme is an e-learning initiative of the EAPCI.

Made it! Tour de Coeur arrives in Barcelona

After a week in the saddle, a team of 35 cycling Swiss heart specialists arrived on time in front of the Fira Gran Via yesterday. Their 760 kilometre route from Geneva had crossed the famous Alpine passes of the Tour de France, all in aid of the Swiss Cardiology Foundation. 'Fantastic,' said Professor Hans Rickli. 'Better to do exercise than to talk about it.'

Don't Miss

- **08:30 - 18:00** **Skopje (The Hub) - Central Village**
  A Day with the Legends
- **08:30 - 18:00** **Brussels - Central Village**
  Global Focus Sessions Live & Recorded cases
- **08:30 - 18:00** **Brussels - Central Village**
  Mobile App Interactive Sessions throughout the Villages, Cases in Crossfire, Meet the Experts, Guidelines in Daily Practice
- **08:30** **Barcelona - Central Village**
  Hot Line: Cardiovascular disease: novel therapies
- **10:10** **Brussels - Central Village**
  The European Heart Journal's Year in Cardiology: heart failure and valvular heart disease
- **10:10** **Central Village in Hubs**
  Meet the Trialists
- **11:00** **Barcelona - Central Village**
  ESC Guidelines 2014 overview
- **12:40** **Central Village the Hubs**
  Young Investigators Awards sessions
- **12:40** **Pristina - Village 8**
  Nursing and Allied Health Professionals Investigator Award
- **14:00** **Barcelona - Central Village**
  ESC/EACTS Guidelines on myocardial revascularization
- **16:30** **Barcelona - Central Village**
  Hot Line: Coronary artery disease and lipids
- **16:30** **Podgorica - Village 2**
  Basic and Translational Science Hot Line on Cardiac Disease

Three ESC gold medallists for 2014

Sir Rory Collins, Petr Widminský and Alain Carpentier receive ESC honours

Professor Sir Rory Collins

It is now more than a decade since the first results of the Heart Protection Study were published in *The Lancet* showing that lowering levels of LDL-cholesterol in a wide range of patients with pre-existing vascular disease or diabetes, irrespective of their starting cholesterol level, would lower their risk of subsequent cardiovascular events, results subsequently confirmed by the Cholesterol Treatment Trialists' collaborative meta-analyses from the major statin trials. The leader of these two projects is the recipient of an ESC Gold Medal this year, the Oxford epidemiologist Professor Sir Rory Collins.

'The Heart Protection Study helped revolutionise the way cholesterol-lowering drugs are used,' says Collins, who received his ESC Gold Medal at yesterday's Opening Ceremony. 'Until then, the benefits of statins were thought likely to be restricted to those with elevated cholesterol levels. But the Heart Protection Study showed that the risks of heart attacks and strokes could be reduced with statin therapy even in patients with cholesterol levels in the "normal" range. That really changed the landscape.'

Controversy this year has centred on extending statin therapy to those at a lower risk of CVD, and the balance of side effects and benefit in such individuals as a result. For example, the National Institute for Health and Care Excellence (NICE) in the UK proposed reducing the threshold for statin therapy from a 20% CVD risk over ten years to a 10% risk. The evidence, said NICE, was 'overwhelming', before confirming this change in its latest recommendations.

Collins publicly supported the NICE position - results published from the Cholesterol Treatment Trialists' collaboration in 2012 showed that the benefits of statin therapy outweighed the hazards even in these lower risk individuals. But there were also objections to NICE's proposal, notably in two reports in the *BMJ* which included claims that statin side effects occur in as many as 18-20% of patients. Collins pointed out a serious error in that particular claim to the editor of the journal and, after a six month delay, the authors of the two papers were required to withdraw it. The two papers were not withdrawn by the journal.

Today, mortality trends in most developed countries show steep and consistent declines in premature death from heart disease and stroke and, in the UK, vascular mortality rates in middle age have, remarkably, fallen by more than half in the past three decades. The Clinical Trial Service Unit (CTSU), of which Collins and Professor Sir Richard Peto have been co-directors for more than 20 years, has made substantial contribution to these trends in its major studies of statins, smoking, blood pressure, aspirin and streptokinase. Among the other influential trials performed by the CTSU - from a 30-year catalogue of major trials - is the 1988 ISIS-2 trial of antiplatelet and thrombolytic treatment in acute MI.

Today, Collins and his colleagues continue to emphasise the need for large-scale observational and randomised evidence about the prevention and treatment of major diseases. Indeed, it was the CTSU in the 1980s which pioneered the concepts of mega-trials and meta-analysis in vascular disease, and by so doing demonstrated that even modest effects on major health outcomes in widely prevalent conditions could have dramatic public health consequences.

Collins, who was knighted in 2011 for his services to science, is clearly no stranger to honours, but he describes his inclusion on the list of cardiology luminaries who have received the ESC Gold Medal as 'humbling'. 'For someone working in the field of cardiology,' he says, 'it's the ultimate recognition.'

This year's three ESC Gold Medallists pictured after their awards at yesterday's Inaugural Session. From left to right, Sir Rory Collins, Alain Carpentier and Petr Widimský.

Professor Alain Carpentier

Innovations throughout the career of cardiac surgeon Alain Carpentier, the father of modern mitral valve repair and another of this year's three ESC Gold medallists, have included the Carpentier-Edwards heart valve and more recently the first bioprosthetic artificial heart. 'An award like this provides a real boost to keep doing what you do,' says Carpentier, from the Hôpital Européen Georges Pompidou in Paris.

It was while doing his surgical residency in 1964 that Carpentier began research on biological heart valves. A few weeks after implanting the Starr-Edwards valve (a silicone ball enclosed in a cage), a clot formed on the device from which his patient suffered a stroke. Pledging to solve the problem of clot formation, Carpentier acquired training in chemistry (obtaining his Chemistry PhD in 1975) which allowed him to demonstrate that treatment of animal tissue with glutaraldehyde reduced immunogenicity.

Aiming to create tissue devices which could be inserted as simply as mechanical valves, Carpentier went on to mount his porcine tissue valves in Teflon-coated metallic frames, coining the term 'bioprosthesis'. Implanting the first patient with his 'home made device' in March 1968, he later worked with the Edwards laboratory, which would commercialise the product.

Next Carpentier became convinced that, in the mitral position, surgical techniques preserving the native valve were superior to valve replacement. His key innovation, detailed in his landmark 'French Correction' paper, was the Carpentier-Edwards ring, which stabilises and reshapes the structure holding the valve, allowing patients to keep their own valves. The advance has been widely credited with ushering in the modern era of valve reconstruction.

Carpentier's current endeavour is to develop a bioprosthetic artificial heart as a permanent implant and not just a 'bridge' to transplant. The CARMAT device (representing a contraction of Carpentier and the manufacturer Matra) combines animal tissue with sensor technology adapted from guided missiles. The device, which can be totally implanted within the patient's pericardial sac, has sensors to detect increased pressure, allowing internal control systems to adjust blood flow during exercise.

The first human implantation was performed by Carpentier together with Christian Latrémouille and Daniel Duveau in a 75-year-old patient suffering from end-stage heart disease in December 2013. Although initially successfully, the patient died two and a half months later from failure of an electronic component. The company has since overcome the problem and now plans to undertake three further implantations in terminal heart failure patients with no other options.

Retirement, says Carpentier, who has just celebrated his 81st birthday, is the option of defeated generals. 'I see no reason to stop operating if you remain physically fit,' he says. 'Experience gives surgeons enormous advantages and you have the responsibility to pass knowledge on to the next generation.'

Professor Petr Widimský

Petr Widimský, the Czech Republic cardiologist who was awarded the ESC Gold Medal yesterday, has arguably done more than anyone to promote primary PCI through his series of PRAGUE studies and the ESC 'Stent for Life' initiative.

'The ESC Gold Medal represents the height of my professional career,' he says. 'But it isn't just a personal honour - the award acknowledges the achievements of a great many co-workers who took part in the PRAGUE studies.'

This recognition from the ESC is also particularly special for Widimský, whose father Jiri Widimský was an ESC Board member and Vice-President.

Now, there is an element of nostalgia in his return to Barcelona, for it was here at the ESC Congress in 1999 that Widimský presented his landmark PRAGUE 1 study showing the superiority of immediate PCI over thrombolysis in acute MI patients. 'With the great expansion of cardiology services in the Czech Republic, we had the advantage of a young workforce willing to get up in the night to perform angioplasty,' recalls Widimský, then as now from Charles University Hospital in Prague

When PRAGUE 2 confirmed the results in 850 patients from 51 participating hospitals this fully convinced Czech health providers of the benefits of a primary PCI programme throughout the whole country. A dramatic decline in STEMI mortality followed, which in turn encouraged the Czech Society of Cardiology to publish the first guidelines in 2002 and define primary PCI as the default perfusion strategy.

The idea of the 'Stent for Life' initiative, which Widimský launched with William Wijns in 2008, was to encourage equal access to PCI interventions throughout Europe and bring everyone up to the high standard set by the Czech Republic. A survey had shown that the use of primary PCI ranged from as high as 92% of MIs in some countries to as low as 5% in others. The project identified barriers to guideline implementation, and provided bespoke plans to meet the specific needs of different countries.

A later survey showed a doubling between 2007 and 2011 in use of PCI in six target countries (Bulgaria, France, Greece, Serbia, Spain and Turkey). 'But there's no room for complacency,' said Widimský. 'We're now looking to reduce time delays across Europe and beyond.'

Following the success of PRAGUE 1 and 2, Widimský realised that the same efficient infrastructure might be used to answer other investigator-led questions in cardiology. To date 19 different PRAGUE studies have been launched, 12 completed and two more (PRAGUE 20 and 21) are currently in planning. Taken together, it means that Widimský should be presenting PRAGUE data in ESC Hot Line sessions for many years to come.

ESC guidelines on myocardial revascularisation

By Stephan Achenbach
University of Erlangen-Nürnberg
Germany

MYOCARDIAL revascularisation – by percutaneous coronary intervention (PCI) or surgical placement of coronary artery bypass grafts (CABG) – is one of the most important treatment principles in cardiology. However, both the identification of patients who require revascularisation and selection of the method to achieve restored blood flow must be carefully performed in order to maximise benefit and avoid procedures that do more harm than good.

This is also an area undergoing tremendous research and development efforts. New data are continuously generated and published as diagnostic and therapeutic methods are refined. Thus, it is increasingly recognised that lesion-specific ischaemia must be considered very strongly when selecting revascularisation targets, surgical procedures can be performed at lower risk, and newer stent generations have demonstrated improved outcome over earlier ones.

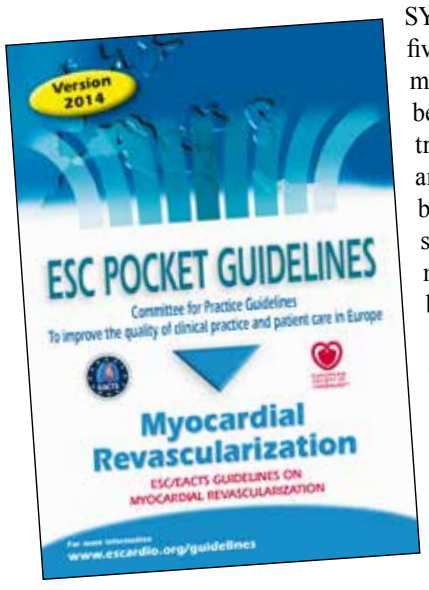
For this reason, the new Guidelines on Myocardial Revascularization, jointly developed and published by the ESC and European Association for Cardio-Thoracic Surgery (EACTS) under the leadership of Stephan Windecker and Philippe Kolh, are particularly relevant and will heavily influence care throughout Europe and beyond.

The 2014 guidelines build on the previous version published in 2010 and cover the selection of patients who require revascularisation, the methods recommended in patients with stable CAD and acute coronary syndromes, revascularisation strategies in specific patient subgroups (eg, patients with diabetes and renal failure), as well as procedural aspects of CABG and PCI and adjunctive medical therapy.

On the selection of individuals who require revascularisation in stable CAD, heavy emphasis is placed on the documentation of ischaemia; FFR measurement carries a Class I recommendation if non-invasive proof of ischemia is not available. For prognostic reasons, revascularisation of left main stenoses, proximal LAD stenoses, stenoses in two- or triple-vessel disease with impaired LV function is recommended, provided there is lesion-specific evidence for ischaemia by FFR or non-invasive testing for lesions that measure less than 90% diameter stenosis. Revascularisation is also recommended for any other stenoses causing ischaemia of 10% or more of the left ventricle.

Finally, revascularisation for symptoms is recommended for all stenoses which cause ischaemia and symptoms which cannot be relieved by medical therapy.

There are substantial changes from the previous version on the method of revascularisation. This is mainly because of the longer-term outcome data generated by the SYNTAX trial (up to five years, with no mortality difference between patients treated by CABG and patients treated by PCI in most subgroups) and that more evidence has become available for new generation drug-eluting stents (which have thinner struts, polymers with better biocompatibility and more effective antiproliferative medication than earlier stents). Consequently, PCI is now regarded as equivalent to CABG in several lesion subsets which previously were recommended as preferably treated by surgery. This includes single- and two-vessel disease with proximal LAD involvement, as well as left main disease and triple vessel disease, provided the SYNTAX score is ≤22. Both CABG and PCI now have a Class I recommendation in these situations.



It remains important to point out that complete revascularisation should be achieved in multi-vessel disease, so that PCI is not recommended (Class III) if anatomy is complex and complete revascularisation cannot be achieved.

The new guidelines also cover in great detail adjunctive pharmacotherapy and medical treatment after revascularisation. This includes those clinically challenging patients in whom dual antiplatelet therapy may be required in addition to oral anticoagulation. For example, in patients with high bleeding risk the guidelines make a Class IIa – Level C recommendation to limit triple therapy to one month, followed by a combination of oral anticoagulation plus either ASA or clopidogrel, both after BMS and DES.

The guidelines cover other specific clinical situations in great detail and offer invaluable help for decisions on the care of patients considered for revascularisation.

The Task Force and their chairmen have performed a marvellous job in this central subject of cardiac care, and the 2014 joint ESC/EACTS guidelines will certainly be most welcome and heavily used by cardiologists and cardiovascular surgeons in Europe and around the globe.

31 August, 14:00-15:30
Barcelona - Central Village
ESC/EACTS Guidelines on myocardial revascularization

New in Barcelona: a battery-free pacemaker, local anaesthesia in TAVI, and mapping AEDs

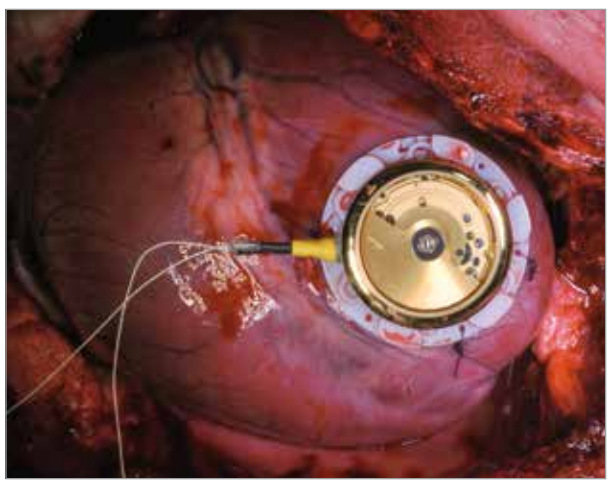
DRAWING ON THEIR clock-making heritage, Swiss scientists are adapting technology from automatic watches to power pacemakers with nothing more than the motion of the beating heart. Their animal experience of 'batteryless' pacing will be described in an Abstract Session today.

'Pacemakers have two weak spots,' explained Adrian Zurbuchen, from the University of Bern. 'Leads are prone to fracture and the lifetime of batteries is limited. Replacing batteries with alternative power sources would spare patients from repeated interventions and make leads obsolete.'

He explained that an automatic watch 'harvests' its energy from the wrist by transforming mechanical energy into electrical energy. Thus, attaching a pacemaker to the epicardium would allow the same system to be directly exposed to the accelerations of myocardial muscle. The motion of the heart winds a spring which accumulates mechanical energy.

In today's study the harvesting device was extracted from an automatic wrist watch and encased in plastic housing with eyelets to allow suture to the epicardium of a 60 kg pig. Results showed that the device generated a mean output power of 52 microwatts - the energy consumption of modern pacemakers is known to be around 10 microwatts.

'This answers our core question that heart motion can be converted into electrical energy that exceeds power requirements of modern pacemakers,' said Zurbuchen, whose group now plans to reduce the size and weight of the prototype to make it more sensitive to heart motion. Zurbuchen added that the technology has potential for use in a multitude of devices, including defibrillators, loop recorders and drug delivery pumps.



Battery-free pacemaker: the energy-harvesting prototype located on the left ventricle (antero apical).

Adrian Zurbuchen: Bid to make pacemaker leads obsolete.

Romain Chopard: Local anaesthesia safe for TAVI?

LOCAL ANAESTHESIA (LA) is as safe and effective for TAVI as general anaesthesia (GA), according to new registry results. Initially TAVI procedures were cautiously performed under GA, but, with growing experience, more heart teams are switching to LA. This is considered suitable for the transfemoral route, but not for transapical and transaortic routes, which require mini thoracotomy and sternotomy.

In a study to be presented on Tuesday, Romain Chopard and colleagues recorded outcomes for 2871 consecutive patients undergoing TAVI in 34 French centres in the FRANCE 2 registry between January 2010 and December 2011. They showed that implantation was considered 'successful' in 97% of patients receiving LA and 97.6% receiving GA (p=0.12); immediate mortality occurred in 3.6% of patients in the LA group and 2.8% in the GA group (p=0.30); and the duration of hospital stay was 9.8 days in the GA group and 8.8 days in the LA group (p<0.001).

Over time there was a progressive increase in the use of LA, which rose from 32% of registry procedures in the first six months to almost 50% in the last six months.

'The advantages of performing TAVI under local anaesthetic includes more accurate clinical assessments of patients during the procedure, optimisation of the TAVI process and enhanced patient recovery,' said Chopard, from University Hospital of Besancon, France. 'Our results would argue in favour of considering wider use of LA, even among high risk patients undergoing TAVI with transfemoral access.'

'GEOGRAPHIC OPTIMISATION modelling' can be used for identifying the best locations for automatic external defibrillators (AEDs), according to French investigators. 'Systematic placement in well known and accessible public facilities accompanied by public information campaigns would make lay rescuers much more aware of AED locations,' said Benjamin Dahan, from Paris Sudden Death Expertise Center, INSERM.

Currently, there is no standardised approach for optimal placement of AEDs. North American guidelines recommend sites with a 'high likelihood of witnessed cardiac arrest'; European guidelines suggest locations where out-of-hospital cardiac arrests (OHCAs) occur at least once every two years.

In their study reported yesterday in an Abstract Session, Dahan and colleagues identified all the OHCAs managed by the Paris Emergency Medical Services between 2000 and 2010, and calculated median distances between the events and a range of different potential locations for AEDs.

Results showed that, of the 4176 OHCAs recorded, 1415 (34%) took place outside the home; 1355 had identifiable geographic co-ordinates amenable to mapping in geographic information systems. The median distance between OHCA and different locations was 324 metres for post offices, 239 metres for subway stations, 137 metres for bike-sharing stations and 142 metres for pharmacies.

'Despite the high number of pharmacies in Paris, their irregular distribution doesn't make them the best candidates for AEDs,' said Dahan. 'Instead we preferred public facilities like metro stations or bike-sharing stations. They also have the advantage of good visibility and public accessibility at night and during weekends.'

31 August, 11:00-12:30
Vilnius - Village 9
A batteryless cardiac pacemaker powered by cardiac motion

2 September, 11:00-12:30
Valetta (The Hub) - Central Village
Safety and efficacy of local versus general anaesthesia in patients undergoing transcatheter aortic valve implantation using a transfemoral approach: VARC-defined outcomes in the FRANCE 2 registry,

After the Mediterranean diet, now try a Nordic diet

THE NEW NORDIC DIET, specially created to bridge the sometimes conflicting interests of health, gastronomy and sustainability, offers the potential to help weight control and reduce blood pressure, according to a study reporting today at a Symposium on cardiovascular prevention.

The diet, Thomas Meinert Larsen will explain, was first developed after Danes described difficulties integrating a Mediterranean diet into their regular eating habits. Thus, the OPUS project was devised to create a healthier and more sustainable food environment for Denmark, with emphasis on palatability and gastronomic potential. The dietary components of the Nordic diet recipes were developed by chefs from the acclaimed Copenhagen restaurant Noma (now designated the best restaurant in the world), who were selected because of their distinct Nordic identity and their consideration for the environment.

The diet comprises 15 food groups: fruit and vegetables (especially berries, cabbages, root vegetables and legumes), potatoes, fresh herbs, plants and mushrooms gathered from the wild, nuts, whole grains, meats from livestock and game, fish, shellfish and seaweed. Typical recipes include baked cod with celery, sweet water pike grilled with summer cabbage and turbot in bread crumbs.

'Our view is that eating foods in accordance with the seasons makes us less dependent on transportation,' said Meinert Larsen, from the University of Copenhagen. 'There's particular emphasis on foraged foods because they taste better, and usually contain greater amounts of vitamins and minerals than conventionally grown plants.'

In the Shop in OPUS (SHOPUS) study 181 men and women with central obesity (defined as waist circumferences >94 cm for men and >80cm for women) were randomised for 26 weeks to the Nordic diet (n=113) or the average Danish diet (n=68), whose macronutrient composition was designed to match diets commonly eaten by adult Danish populations as defined by the latest survey of dietary habits in Denmark.

Those randomised to the Nordic diet received a cookbook with 180 recipes with three menu plans for each season, while those randomised to the Danish diet received a cookbook with 99 recipes but no menu plans - since seasonal variation was not important. 'One innovative aspect of the study was that all ingredients were provided free of charge at a special shop,' Meinert Larsen told *Congress News*.

Thomas Meinert Larsen: recipes developed by chefs from the acclaimed Noma restaurant.

Results showed that the mean weight change was a loss of 4.7 (±0.5) kg for the Nordic diet group and a loss of 1.5 (±0.5) kg for the Danish group (P<0.001). Furthermore, the Nordic diet produced greater reductions in systolic (-5.1 mm Hg) and diastolic blood pressure (-3.2 mmHg) than the Danish diet.

At the population level such reductions are likely to be important, said Meinert Larsen, since even small long-term blood pressure reductions will reduce cardiovascular mortality. The concept of a healthy, regional, sustainable, seasonal and highly palatable diet, he added, could in principle be applied anywhere in the world, not just Nordic countries.

31 August, 8:30-10:00
Berlin - Village 8
Cardiovascular prevention – the role of diet and weight control

Childhood hypertension: the case for vigilance is now 'stronger than ever'

JUST AS CHILDHOOD obesity is directly associated with obesity in adulthood, so evidence is growing that blood pressure in childhood predicts blood pressure in adulthood. The difference, of course, is that the one is much more evident than the other.

However, according to the fourth report from the National High Blood Pressure Education Program (NHBPEP) Working Group on Children and Adolescents published in the USA in 2004, 'primary hypertension is detectable in the young and occurs commonly' - even though the majority of cases still remain undiagnosed.

Detection has been helped in recent years by the development of a reliable database of blood pressure levels in childhood, which have allowed the calculation of BP levels for each sex and age group and for seven height percentile categories.

'Blood pressure in children increases with age and body size,' explains Empar Lurbe, Professor of Pediatrics at the University of Valencia, who will speak this morning at a Symposium on hypertension in the young. 'This makes it impossible to use a single blood pressure level to define hypertension, as we do in adults.'

Thus, hypertension in children is now defined as systolic and/or diastolic BPs persistently higher than or equal to the 95th percentile specific for age, sex and height, measured on at least three separate occasions. Normal BP is defined as systolic and diastolic BPs less than the 90th percentile. Children with an average systolic or diastolic BP of the 90th percentile or more but less than the 95th percentile are classified as having high-normal blood pressure.

During this morning's Symposium Lurbe will call for greater efforts in identifying and treating children and adolescents with high blood pressure - and treatment, she will claim, requires specific approaches dependent

Empar Lurbe: 'The problem of childhood hypertension is already with us, and it continues to grow.'

on circumstances, target BPs, and the presence of characteristic mechanisms likely to benefit from particular antihypertensive agents. Chronic kidney disease, diabetes mellitus, metabolic syndrome and heart failure are among the most common.

Most cases of high-normal BP and hypertension in childhood are not cases of secondary hypertension to be detected and treated specifically, but rather the result of lifestyle. 'Being overweight is probably the most important of the conditions associated with elevated BP in childhood,' says Lurbe, 'and accounts for more than half the risk for developing hypertension. First, we should understand these conditions in order to return blood pressure to within the normal range and prevent high levels in youth developing into full hypertension in adulthood.' Any intervention that reduces energy intake and increases physical activity in these children is likely to be helpful in lowering their BP.

Because cardiovascular endpoints such as MI, stroke, renal insufficiency or heart failure are extremely uncommon in childhood, their rarity has so far prevented event-based randomised therapeutic trials.

However, 'clinical experience' suggests to Lurbe that a reduction of high BP in life-threatening conditions, such as acute heart failure, hypertensive encephalopathy or malignant hypertension, does improve survival and reduce sequelae in children.

Lurbe advises that any pharmacological treatment should be started with a single drug. 'When blood pressure does not respond adequately or significant side effects occur,' she says, 'switching to another antihypertensive drug of a different class is recommended.

This procedure allows detection of the patient's best individual response to the drug in terms of efficacy and tolerability. As the response rate is often not sufficient in single-drug treatment, particularly in moderate or severe hypertension, combination therapy is often necessary.'

The 'problem' of childhood hypertension is already with us, says Lurbe, and it continues to grow. Estimates suggest that around 3% of those aged between 3 and 18 years have high-normal BP, and around 3% are hypertensive. Moreover, one study from 2007 estimated that the combined prevalence of 'prehypertension' and hypertension in obese adolescents was above 30% in boys and 23-30% in girls. With high blood pressure in childhood now directly linked to hypertension in adulthood, and adult hypertension the leading cause of premature death around the world, the case for BP vigilance in children seems stronger than ever.

31 August, 11:00-12:30
Prague - Village 3
Hypertension in the young

Stress and natural disasters may pose high risks for coronary artery spasm

William Harvey lecture today on research in coronary spasm

IN THE WILLIAM HARVEY Lecture this morning Hiroaki Shimokawa will urge cardiologists to pay more attention to coronary artery spasm. The condition, he says, can sometimes be overlooked by cardiologists in the West, who are often cautious about provocation tests.

'We used to think the incidence of coronary spasm was three times higher among Japanese populations than Caucasians,' he explains. 'But now we believe the incidence probably isn't that different – it's just that Western cardiologists are less likely to perform the tests.'

Diagnosing coronary spasm, adds Shimokawa, who is director of the Cardiovascular Centre at Tohoku University Hospital, Japan, is of vital importance as a trigger of myocardial ischaemia in patients with and without obstructive CAD and may result in life-threatening ventricular arrhythmias.

In today's lecture Shimokawa will provide an overview of his translational research suggesting that Rho-kinase has a crucial role to play in the pathogenesis of coronary spasm. Rho-kinase enhances myosin light chain phosphorylation through inhibition of myosin-binding subunits of myosin phosphatase, leading to vascular hyperconstriction or vasospasm.

In his studies, Shimokawa has been greatly helped by the first ever animal model of coronary spasm. The porcine model, which he developed in 1983, used a combination of balloon damage to the endothelial cells followed by high-

Hiroaki Shimokawa: 'Our research suggests new approaches to the treatment of vasospasm.'

cholesterol feeding. After six months, Shimokawa was able to induce spasm by intracoronary histamine or serotonin, and show that inflammatory changes of the coronary artery play an important role in its pathogenesis in pigs.

Using the porcine model, Shimokawa and his group showed significant correlations between the extent of myosin light chain phosphorylation and vascular smooth muscle contractions. 'We believe Rho-kinase activation plays a major role as the molecular switch that triggers not only coronary artery spasm but also atherosclerosis in general,' he explains.

In clinical studies Shimokawa showed that the selective Rho-kinase (ROCK) inhibitor, fasudil, prevents myocardial ischaemia in patients with coronary spasm. Furthermore, he showed that Rho-kinase activity in circulating neutrophils provided a useful biomarker for diagnosis and disease activity assessments in patients with vasospastic angina. At the molecular level, he has also demonstrated that Rho-kinase downregulates the enzyme endothelial nitric oxide synthase. In a separate series of experiments, he showed that endothelial nitric oxide synthase provides a source of hydrogen peroxide, which in turn he found to be the substance responsible for dilating small resistance vessels as an endothelium-derived hyperpolarising factor.

'Taken together,' he says, 'our research suggests new approaches to the treatment of vasospasm. You can give drugs like fasudil to suppress Rho-kinase activity or promote healthy levels of endothelial nitric oxide synthase through exercise, female hormones and ACE inhibitors.'

Shimokawa believes that psychological stress also plays a major role in coronary artery spasm. In the studies he undertook in patients with coronary artery spasm following the 2011 Great East Japan Earthquake (which he experienced first hand), Shimokawa showed that Rho-kinase activity in the circulating neutrophils of patients with vasospastic angina correlated with post traumatic stress disorder scores six months after the event.

'In separate research, we showed that cardiovascular events rose after the disaster and, taking these studies together, it's conceivable that transient enhanced coronary vasospastic activity increased the number of fatal arrhythmias,' he says. 'Clinicians need to be made aware that patients may be at greatest risk of suffering spasm at times of natural disaster or psychological stress.' The mechanisms for Rho-kinase activation during stress, he adds, remain to be clarified.

For such situations, Shimokawa firmly believes that it is important to identify those patients at greatest risk. Working with the Japanese Coronary Spasm Association, he developed a database of nearly 1500 patients with coronary spasm and from their outcomes used a multivariable model to select seven variables representing predictors of major adverse events. 'Ultimately this model should help us decide who to focus on,' he explains. 'Patients found to be at high risk can now be treated with calcium channel blockers, ACE inhibitors and statins.'

Shimokawa feels especially honoured to be the first Japanese scientist invited to give the William Harvey Lecture. 'For Japanese cardiologists the ESC Congress has become our overseas meeting of choice,' he says. 'We find opportunities to take a generalist approach help our translational science and we feel comfortable that not all European doctors speak English.'

31 August, 08:30-09:10
Skopje (The Hub) - Central Village
ESC William Harvey Lecture on basic Sciences

In search of the best treatment strategies in PCI

Today's Andreas Gruentzig lecture to review recent stent trials

IN TODAY'S Andreas Gruentzig lecture Adnan Kastrati will recall his contributions to improving safety and efficacy in restenosis and late stent thrombosis.

'The increased risk for late stent thrombosis with drug eluting stents seems to be the price paid for the dramatic reductions in restenosis,' says Kastrati, Professor of Cardiology at the Deutsches Herzzentrum, Technische Universität, Munich.

Through the ISAR series of studies, which he now directs, Kastrati has made significant contributions to improving stent technology. The Intracoronary Stenting and Antithrombosis (ISAR) Research group, launched in 1994, has undertaken more than 50 randomised controlled studies involving more than 45,000 patients with an overall objective of defining optimal treatment strategies in PCI.

'Three main principles characterise these trials,' explains Kastrati. 'First, simplicity - one question one answer; second, a focus on issues that are relevant for practice; and third, a strong spirit of performing industry-independent studies.'

The first ISAR trial designed by Professor Albert Schömig (Kastrati's mentor) demonstrated that safety of stenting procedures can be improved by replacing oral anticoagulation with dual antiplatelet therapy. 'Together with other trials this study led to an explosion in the number of patients having stents for coronary artery disease,' says Kastrati.

In the era of DES, several ISAR trials including ISAR-DIABETES, ISAR-DESIRE and ISAR-SMART 3

Professor Adnan Kastrati: 'New generation DES have been developed with excellent efficacy and improved safety compared to first generation DES.'

consistently demonstrated superior efficacies for sirolimus-eluting stents over paclitaxel-eluting stents, with the result that limus-based DES are now the standard technology.

'New generation DES have been developed with excellent efficacy and improved safety compared to first generation DES.' says Kastrati. 'With the latest designs we've seen the incidence of stent thrombus at four years halve from 3% with first generation DES to 1.5% with second generation DES.'

Now, in the PRESTIGE (PREvention of Late Stent Thrombosis by an Interdisciplinary Global European effort) project, Kastrati and colleagues are teasing out mechanisms which contribute to late (between 30 days and one year) and very late (>1 year) stent thrombosis. The project includes basic research to elucidate molecular and cellular mechanisms underlying stent thrombosis, a bio-engineering approach to assess new intravascular imaging, and a clinical approach exploring risks for stent thrombosis.

Kastrati's group is evaluating more than 500 subjects, with data collection involving full clinical histories, assessments of original PCI procedures, details of antithrombotic therapies, intravascular imaging and thrombus histopathology, genetic information and platelet function tests.

'Previous studies have been hampered by small sample sizes, incomplete patient characterisation and a lack of detailed intracoronary imaging and thrombus assessment,' he says. 'Our multi-approach strategy and larger numbers will give a better idea of what's going on.'

The project, which is funded by a FP7 grant and involves eight European heart centres, also hopes to develop and validate novel imaging technologies for early diagnosis of events contributing to late stent thrombosis.

'Ultimately we hope to relate these histological imaging markers to outcomes and from this determine the best approach to manage recurrences in individual patients,' he says.

31 August, 09:20-10:00
Skopje (The Hub) - Central Village
ESC Andreas Grüntzig Lecture on Interventional Cardiology

A paradigm of translational medicine

Laennec lecture: The genetic basis of arrhythmogenic cardiomyopathy

IN TODAY'S Rene Laennec lecture Gaetano Thiene will recall the translational research odyssey which led him from studying arrhythmogenic right ventricular cardiomyopathy (ARVC) at autopsy to the discovery of culprit genes encoding proteins at cell junctions.

'In the era of clinical imaging I'll show that pathology is not an old fashioned, useless discipline,' says Thiene, Professor of Cardiovascular Pathology at the University of Padua. It was here that he qualified in 1972 and worked first as a cardiologist and then pathologist. But he was motivated to train as a cardiopathologist after two of his nieces were born with congenital heart defects.

One of Thiene's early achievements was establishing a registry of 2000 specimens from patients with congenital heart disease in most of whom surgery had failed. 'At postmortem we were able to relate failures of surgery to the anatomical variations we found,' he says.

Working with his wife, the pathologist Marialuisa Valente, Thiene discovered that a reaction between calcium and phosphorus which occurs in valve cusps was the main cause of porcine bioprosthetic valve failure. Through the introduction of anti-calcification treatments, the durability of bioprosthetic valves increased two-fold.

Thiene's first fateful encounter with ARVC came in May 1979 when he performed the postmortem of a young doctor who had died suddenly on the tennis court. On autopsy he observed fibro fatty tissue in the RV-free wall, but at time there was no appreciation in pathology that aberrant cardiac electricity could be a cause of death.

Then, as in so many medical breakthroughs, serendipity intervened. The doctor's girlfriend brought to his attention a note in the deceased's diary - 'ventricular tachycardia of left bundle branch block morphology'. Unearthing his ECG, they found a peculiar pattern at rest - T wave inversion on the right precordial surface and left bundle branch block QRS pattern during ventricular tachycardia.

Gaetono Thiene with his wife Marialuisa Valente, who together discovered the cause of failure in porcine bioprosthetic valves.

The observation motivated Thiene to keep careful records of the autopsies of young people who died suddenly in the Veneto region of north-eastern Italy. From 1979 to 1986 Thiene did postmortem studies on 60 consecutive young sudden deaths and found that 12 showed the same morphological features and ECG pattern as the original subject. ECGs had been compulsory in Italy since 1982 for anyone involved in competitive sports. The resulting paper in 1988 in the *New England Journal of Medicine* led to the establishment of ARVC as a major cause of sudden death in he young, which they believed to be familial.

Inspiration to solve the genetic puzzle came from the island of Naxos, where clinicians Nikos Protonoarios and Adalena Tsatsopoulou observed a cardiac malignant disease consisting of both cutaneous and cardiac manifestations. This led to the eventual association of ARVC with desmosomal (cell junction) protein abnormalities, and the identification of molecular defects in the desmosome proteins, including deletion of plakoglobin (found in the recessive Naxos disease) and mutations in desmoplakin (found in the dominant Venetian disease).

Thus, both dominant and recessive variants of AC were eventually identified as cell junction diseases. 'Desmosomes maintain attachment of cardiomyocytes during diastole and systole,' explained Thiene. 'Cardiomyocytes which are not firmly attached in ARVC results in cell death and their replacement by fibro-fatty tissue, which interferes with electrical impulses.'

The discovery of defective genes opened new avenues of research, including experiments in mice models. 'It was fascinating to find mice hearts appear normal at birth, but with the phenomenon of progressive cell death and ventricular fibrillation occurring after a few weeks,' says Thiene.

Such observations, he adds, raise the possibility of finding treatments for children which prevent onset of disease. Indeed, since 10-20% of young people who die suddenly present with normal hearts, says Thiene, molecular autopsy must be performed in these cases. 'Cardiovascular pathologists are needed to take a systematic approach to molecular genetics, to ensure that all mutations are screened for. This provides the critical information to save the lives of relatives at risk of similar fates,' says Thiene.

31 August, 11:00-11:40
Skopje (The Hub) - Central Village
ESC Rene Laennec Lecture on Clinical Cardiology. The research venture on arrhythmogenic right ventricular cardiomyopathy: a paradigm of translational medicine

What in your view is the best innovation in cardiology in the last decade?

Suvankar Ghosh
Interventional cardiologist
Baroda, Valodara, India

"For me the biggest boom in cardiology has been the introduction of primary angioplasty for patients with acute MI. Since the introduction of primary angioplasty we have seen mortality rates for acute MI in my city going down by 25 to 30%. Primary PCI overcomes the complications of thrombolytic drugs such as haemorrhagic stroke and also means that patients don't have to undergo debilitating bypass surgery.

I believe that because we are treating patients so promptly they're less likely to go on to develop long-term complications, such as heart failure. Ultimately this could lead to even greater gains in survival."

Akpa Maclean
Cardiologist from University of Port Harcourt Hospital,
Port Harcourt, Nigeria

"Novel oral anticoagulants for atrial fibrillation for me have had the most impact for patients. Before, we relied on beta blockers, but they weren't ideal and you had to be selective about their use. AF is a big issue in Nigeria, mainly because of poor access to treatment for rheumatic heart disease.

The benefit of the new anticoagulants is that they don't need monitoring and their safety profile for non-valvular AF is good - we've not had patients with bleeding. Now what we hope for is the same indication for valvular disease, to improve the lives of even more patients."

faces in the crowd

Egle Prascience
Third year cardiology resident
Kaunas, Lithuania

"For me it has to be imaging. Advances in imaging technology, such as 3D echo and computed tomography, are providing vital information to help prevent some patients from having some interventional procedures. Computed tomography measures the calcium content of vessels. This means that cardiologists can identify those patients at greatest risk of MI who can be referred for angiography investigations. Others can be treated medically.

Another area is valve surgery where 3D echocardiography is being used to produce images of malfunctioning valves. This can help surgeons plan their operations."

Raghid Khatib
Cardiologist between jobs
Sweden

"For me it's the development of treatments for heart failure and better management of the condition since the introduction of biomarkers. There's also the use of ICDs, VADs and pacemakers. A decade ago these were not available as they are now - nor as advanced or modern. They can also bridge the gap for patients waiting for heart transplants - temporarily or even long-term, given the length of waiting lists for organs. Some people are able to continue their lives on these devices. We've also got better at assessing heart transplant suitability in patients with chronic heart failure and at identifying risk factors."

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Beirut Room
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Sunday, August 31, 2014
(12.45-13.45)

First-line management of hypertension: assessing new strategies

Faculty

George Bakris
Gianfranco Parati
Charalambos Vlachopoulos

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