

SUNDAY 28 AUGUST

A five-year strategic plan to meet the challenges of CVD

THE ESC IS LOOKING to plug the gap between cardiovascular knowledge and routine clinical practice with development of a five year strategic plan, said ESC President Professor Fausto Pinto at yesterday's Inaugural Session.

Despite timelines showing steady declines in CV deaths over the late 20th and 21st centuries - from 430 deaths per 100,000 population in 1950 to 100 per 100,000 in 2010 - Eurostat figures for 2013 show that one in six deaths in the EU can be attributed to avoidable myocardial infarction.

'CVD is still the leading cause of death in Europe and worldwide, and responsible for over four million deaths a year in Europe, close to half of all deaths. The annual cost to the region's economy is estimated at €200 billion,' he said.

In his address Professor Pinto, whose two-year term as ESC President ends on Tuesday, outlined how the ESC believes scientific societies have a fundamental role to play in improving public health. And in tackling these future challenges the five year strategic plan (from 2016 to 2020), will embrace advocacy, research, education, congress and membership.

Drivers of the plan, Professor Pinto explained, include promoting the ESC family as a single, cohesive entity, the ESC becoming the prime source for the professional development of CV healthcare professionals, the ESC being a key facilitator of excellence in research and innovation, and the ESC advocating the highest standards of CV patient care.

'We will have to take into account strategic trends, including a gender flip in which 70% of cardiologists in

training are now women, a generation gap leading to cultural changes, increasing economic pressure on healthcare, a stringent regulatory environment and the IT revolution,' explained Professor Pinto, who is from Lisbon University Medical School.

Key content of the strategic plan includes:

Advocacy: With advocacy, the plan aims to manage the ESC brand, enhance the Society's reputation by training a cadre of experts, and develop all media channels including social media.

Research: With research, the plan aims to encourage excellence and manage research innovation. Key actions here include reinforcement of some currently successful activities, such as the EURObservational

Research Program (EORP), as well as development of an ESC-wide research 'think tank' to help shape the future role of ESC in supporting research.

Education: With education, the aim is to deliver world class learning and professional development. Key actions include developing and implementing an educational blueprint, engaging in state-of-the-art technology and enhanced learning to develop robust educational programmes, and conducting a needs assessment. This will allow future generations to be exposed to the latest educational methods.

Congress: With congress, the aim is to organise successful congresses offering the best scientific content and attracting the



Outgoing ESC President Professor Fausto Pinto: A five-year plan which embraces advocacy, research, education, congress and membership.

best people. Key actions include developing world-class scientific programmes, designing initiatives to engage new audiences and developing a virtual congress concept based on the ESC 365 Programme.

Membership: With membership the aim is to engage all ESC members throughout the world more deeply in the Society's activities. At ESC Congress 2016 an ESC individual membership will be launched, with three membership levels offering a range of benefits, including the new ESC Professional membership and ESC Professional Plus membership (see page 2 for details).

Further information on the new ESC membership is available at the ESC Stand.



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Don't Miss		
07:45 - 08:15	The Hub & the Agora	Science@Breakfast sessions
08:30 - 10:00	Rome (Main Auditorium)	ESC Clinical Practice Guidelines Overview
11:00 - 12:30 / 16:30 - 18:00	Rome (Main Auditorium)	Hot Line Sessions
08:30 - 18:00	Raphael (The Hub)	e-Cardiology track
08:30 - 18:00	Galileo (The Hub)	Gladiators Arena
08:30 - 10:00 / 11:00 - 12:30	Forum (The Hub)	Heart Team Sessions
07:45 - 18:00	Bernini (The Hub)	Scientists of Tomorrow Track
	Michelangelo (The Hub)	Cardiologist of Tomorrow Track
12:40 - 13:50	The Hub	Abstract Awards Sessions

Here again: Tour de Coeur cyclists arrive in Rome

They crossed the Rubicon by bike and, like Swiss railways, arrived in Rome on time from Lugano, Switzerland. The 43 pedalling cardiologists and friends (including two from New Zealand) took seven days for their 750 km annual Tour de Coeur to ESC Congress. 'It's fun, it's healthy and it sets a good example,' said physiotherapist Susanna Gnehm. And the weather this year was perfect.



ESC collection for victims of the Italian earthquake

Donations for the victims of Wednesday's tragic earthquake, which struck a mountainous region 65 miles north-east of Rome, can be made in a collection box located in the Congress Registration area.

It is now known that at least 290 people died and 400 were injured in the disaster. The money raised will be donated to the Italian National Civil Protection Department by ESC Secretary/Treasurer Professor Francesco Cose.

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Collect your **FREE** 2016 Pocket Guidelines at the Registration Area, today from 14:00

Discover your ESC Membership benefits
ESC Stand, ESC Plaza

Two new ESC gold medallists for 2016

Alain Cribier and Bernard Gersh honoured at yesterday's Inaugural Session

They both spoke to *ESC Congress News* about their distinguished careers and about new developments in cardiology.

ESC: How did you first become interested in cardiology?

Alain Cribier: As a medical student I trained in well known departments of cardiology and cardiac surgery in Paris and decided cardiology was a fast developing specialty. After some hesitation I finally opted for cardiology over cardiac surgery.

Bernard Gersh: Cardiovascular physiology was the subject I found most interesting as a medical student at the University of Cape Town. The apparent simplicity of the pump, arteries and electrical system seemed far more tangible than abstract subjects like biochemistry.

ESC: And your most influential mentors?

AC: Albert Scheitzer, who strengthened my teenage conviction to be a doctor; Charles Dubost, a world famous pioneer in cardiac surgery; later in Los Angeles Jeremy Swan and William Ganz, who opened my eyes to research and innovation; finally, Brice Letac, the director of the department of cardiology in Rouen, who pushed me towards research.

BG: Velva Schrire, who established the cardiac clinic at the University of Cape Town, first communicated to me the excitement of clinical cardiology. Cedric Prys-Roberts, my DPhil supervisor at Oxford, taught me about experimental design and how to present, write and analyse data. And from the time I started at the Mayo Clinic, Robert L. Frye has taught me a great deal about both medicine and life.

ESC: What have been your principal scientific and clinical interests?

AC: My first experience with cardiac catheterisation in Paris in 1972 encouraged me to take up invasive cardiology. My interest in developing innovative technologies started 30 years ago. Some ideas failed, others were successful, but the resounding success of transcatheter aortic valve implantation allows me to draw up a positive balance sheet overall.

BG: Many areas of cardiology have truly fascinated me, although staying abreast of all these disciplines has sometimes felt like trying



This year's two ESC Gold Medallists pictured after their awards at yesterday's Inaugural Session. Alain Cribier, left, and Bernard Gersh.

to ride four horses at the same time. Natural curiosity has been responsible for my wandering off into all sorts of different areas. The reperfusion era in MI was an absolute highlight from both the clinical and research perspectives, and I have had long standing interests in atrial fibrillation, clinical electrophysiology, hypertrophic cardiomyopathy, outcomes of surgery versus medical therapy in stable CAD, and more recently stem cells and issues related to CVD in the developing world.

ESC: Of which of your studies/research are you most proud?

AC: Having been able to develop several interventional technologies, and doing so against a background of negative opinions from experts. My three innovations in the field of valve disease, balloon aortic valvuloplasty in 1985, mitral mechanical commissurotomy in 1992, and TAVI in 2002 are my main contributions.

BG: I published a series of papers suggesting AF is not just a rhythm disturbance but the consequence of an interplay of risk factors for vascular disease. I was also involved in the pivotal trial of primary PCI versus thrombolysis and played a role in defining the natural history of HCM. I've always been an advocate of evidence-based medicine, and believe evidence should come from analysing your own experience as well as that of others.

ESC: What have been your greatest professional challenges?

AC: Undoubtedly convincing experts of the benefits of TAVI. The project, which involved

using transcatheter techniques to implant a percutaneous heart valve within the diseased calcified native valve in the beating heart with no general anaesthesia, was dismissed by many as the 'most stupid' idea ever conceived. Who would believe that 14 years after the first-in-man case was performed in Rouen in 2002, 300,000 patients worldwide have been treated with TAVI.

BG: To go from a clinically orientated medical school in South Africa to the academic environment of Oxford University.

ESC: What do you regard as the most significant recent developments in your field?

AC: The development of interventional cardiology for treatment of coronary artery disease, with angioplasty introduced by Andreas Gruentzig in 1977 the landmark event, followed by a number of exciting related catheter interventions, including coronary stenting. Since the early 1980s, the increasing role of interventional cardiology for treatment of congenital and acquired valvular disease, including TAVI, has considerably enlarged the field of transcatheter interventions and catalysed development of other technologies for structural heart diseases.

BG: The phenomenal declines in CVD mortality attributed to identification of risk factors, angioplasty and the implementation of prevention guidelines by national societies.

ESC: Looking into a crystal ball, how do you see your field developing?

AC: I predict the expansion of indications for TAVI to lower risk and younger patients as demonstrated by recent positive results in trials.

It's likely that surgical valve replacement will only be used in patients who are not optimal candidates for TAVI.

BG: The epidemics of diabetes, hypertension and other risk factors pose huge challenges both in the western and developing world. Looking to the future, we need to attack the consequences of our prosperous life styles aggressively through risk factor modifications, which will require massive education programmes and the political will to enact environmental and legislative change.

ESC: What are your future research goals?

AC: My role in innovation is behind me. Instead, I am now interested in educational programmes.

BG: To continue the areas of research I have had for the last 30 years, and spend time helping to get CVD research programmes organised in my old alma mater and other institutions in South Africa.

ESC: What advice would you give to young cardiologists?

AC: I'd quote André Gide: 'One doesn't discover new lands without consenting to lose sight of the shore for a very long time.' In other words, believe in yourself and never be discouraged.

BG: If you have the drive and intellectual ability to combine clinical work, education and research, this is an incredibly stimulating career and lifestyle opportunity, albeit a busy one. My advice is, don't worry about change because it will inevitably happen and you will adapt to it.

ESC: What has your involvement been with the ESC over the years?

AC: I have been a Fellow of the ESC for 30 years attending each congress - as invited faculty in most of them - and I gave the 2010 Andreas Gruentzig Lecture in Stockholm.

BG: I am one of the deputy editors of the *European Heart Journal*, have been on the ESC Guideline Committee on Unstable Angina, and gave the Rene Laennec Lecture in 2010.

ESC: What does the ESC medal mean to you?

AC: Receiving this prestigious award is a privilege and great honour. It's gratifying to be recognised for my efforts in developing new medical technologies.

BG: I'm really thrilled by this totally unexpected honour. It's a highlight of my career. Awarding the ESC Gold Medal to non-Europeans emphasises the worldwide fraternity of academic cardiology.

A special membership offer for ESC Congress delegates

A new ESC membership scheme is launched at ESC Congress 2016, in which healthcare professionals have the opportunity to become ESC Professional Members or ESC Professional Plus Members.

As a delegate at ESC Congress, you are part of the ESC family. To show commitment to this community, ESC is pleased to offer a one-off complimentary ESC Professional Membership to eligible participants. This special introductory launch offer gives free access to ESC Professional Membership benefits from now until 31 December 2017 – a full 16 months.

ESC Professional and Professional Plus Memberships can add value to your daily clinical practice. To make the most of your ESC membership benefits, visit the ESC Stand in ESC Plaza to learn more and see demonstrations of the e-learning platform, and online journal access.

As an ESC Professional Member or ESC Professional Plus Member, you receive numerous benefits over and above ESC Members:

- Discounts on ESC Congress registration

- Annual online subscription to your choice of *European Heart Journal* or *Cardiovascular Research* (ESC Professional Members) or both (ESC Professional Plus Members)

- Annual print subscription to *European Heart Journal*, *Cardiovascular Research*, or *European Journal of Cardiovascular Nursing* (ESC Professional Plus Members)

- Up to 60% off the annual print subscriptions to ESC family journals including *European Heart Journal*, *Cardiovascular Research*, *European Journal of Cardiovascular Nursing*, *EHJ: Pharmacotherapy*, and *EHJ: Quality of Care and Clinical Outcomes*
- Further discounts on educational materials including ESC General Cardiology textbooks, Summary cards for General Practice, Essential messages from ESC Guidelines, and ESC Pocket Guidelines

- Half price (ESC Professional Members) or free access (ESC Professional Plus Members) to the General Cardiology Continuing Professional Development Programme on the ESC eLearning platform.

These two new individual ESC memberships are completely new. The special introductory launch offer of a complimentary ESC Professional Membership is available only to ESC Congress delegates. Don't miss your chance to be part of a valued cardiology community of peers and start accessing the many privileges now.

16-month ESC Professional Membership for ESC Congress delegates. Visit the ESC Stand in ESC Plaza to find out more about the complimentary 16-month ESC Professional Membership for ESC Congress delegates.

If your badge says ESC Member or ESC Professional Member, pick up your FREE 2016 ESC Pocket Guidelines from 14:00 today in the registration area.

The management of atrial fibrillation: multidisciplinary input for new joint guidelines from ESC and EACTS



By Stefan Agewall
Oslo University Hospital Ullevål
Oslo, Norway



and John Camm
St George's University of London
and Imperial College London

THE NEW ESC/EACTS Guidelines for the management of atrial fibrillation are presented during this congress. The work has been led by Paulus Kirchhof and Stefano Benussi and is a full rewrite following on from the 2010 and 2012 guidelines on atrial fibrillation

What's new?

The 2016 *Atrial Fibrillation* guidelines reflect the increasing need to integrate and coordinate the care of AF patients. This is reflected in the multidisciplinary input of the Task Force, which included expert cardiologists and electrophysiologists, stroke neurologists, specialist AF nurses and cardiac surgeons.

There is now more emphasis on early detection of asymptomatic 'silent' AF. Diagnosis of AF requires an ECG (IB evidence), with the value of atrial high rate episodes picked up by implanted devices unclear at present. Silent, undiagnosed AF is a common cause of stroke, and the guidelines recommend both opportunistic and targeted intensive ECG screening for AF in all patients over

the age of 65 or those with stroke or transient ischemic attack (IB)

Oral anticoagulation remains a major treatment component in AF, and, apart from patients at the lowest risk of stroke (women and men without any clinical risk factors), most others will derive a net clinical benefit from anticoagulation (IA).

Patients with a single stroke risk factor (CHA2DS2-VASc score of 2 for women and 1 for men) should be considered for anticoagulation, taking account of individual characteristics and patient preferences (IIaB); men with a CHA2DS2-VASc score of 2 and women with a score of 3 should be recommended for anticoagulation (IA). Non vitamin-K oral anticoagulants (NOACs) are now recommended as the first-line anticoagulant in eligible patients (IA) as a result of their better safety profile.

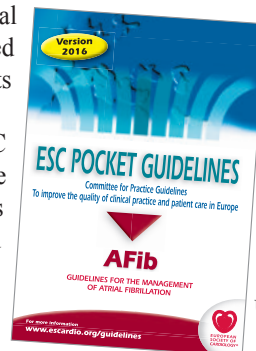
Patients who are ineligible for NOAC therapy, such as those with moderate-severe mitral stenosis, mechanical heart valves and severe chronic kidney disease, should be treated with vitamin-K antagonists, maintaining a high time in therapeutic range (IB). Aspirin and other antiplatelets have no role in stroke prevention (III A).

Preventing major bleeding events in anticoagulated AF patients is extremely important. To reduce the risk of bleeding, the guidelines provide a list of modifiable bleeding risk factors that clinicians should minimise in anticoagulated patients, but a specific bleeding score is no longer recommended. Importantly, bleeding and stroke risk factors overlap and patients at high risk of bleeding are likely to benefit from anticoagulation (IIaB).

The guidelines also provide suggestions for initiation and/or resumption of treatment after ischaemic strokes and after intracranial haemorrhage. These difficult decisions should be taken by interdisciplinary teams.

Symptoms should be assessed by the modified EHRA score (IC), including AF-related tiredness and breathlessness, which are common symptoms in AF patients.

Catheter ablation is now reaching the mainstream of AF management and data underpinning its use have expanded in number and quality. Catheter ablation is the rhythm control therapy of choice in patients with symptomatic recurrences of AF on anti-arrhythmic drug therapy (IA paroxysmal; IIaC persistent), and emerges as a valid first-line alternative to anti-arrhythmic drugs in selected patients with symptomatic paroxysmal AF (IIa B).



• To support clinical decision making in line with the 2016 atrial fibrillation guideline, new state-of-the-art tools are available in the ESC Pocket Guidelines app. These include an overall treatment manager which has been developed by the EU-funded project CATCH ME.* These impressive features, which are both novel and intuitive, will help healthcare professionals personalise prevention and management of their AF patients and implement best clinical practice, even when under pressure to make a rapid decision.

• *CATCH ME (Characterising Atrial Fibrillation by Translating its Causes into Health Modifiers in the Elderly, www.catch-me.info) brings together the expertise of leading academic institutions, healthcare organisations and professional societies with an aim to improve the care of patients with AF.*

Don't miss :

What is new in the 2016 atrial fibrillation guidelines?
28 August 14:00-15:30 Rome - Main Auditorium
Meet the guidelines Task Force - atrial fibrillation
28 August 15:45-16:15 Forum - The Hub

NOACs and cardioversion: the experts talk

Satellite Symposium - Experts on the Spot

Sunday, 28 August 2016
10:15-10:45
Michelangelo - The Hub

10:15 WELCOME AND INTRODUCTION
Professor Raffaele De Caterina, Italy

10:20 NOACs IN CARDIOVERSION: CURRENT LANDSCAPE
Professor Andreas Goette, Germany

10:25 ENSURE-AF: EDOXABAN IN SUBJECTS UNDERGOING CARDIOVERSION
Professor Gregory Lip, UK

10:30 PANEL DISCUSSION AND CONCLUSIONS
All



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Two specialties with one common goal

Romanian cardiologist Dan Gaita on the cardio-diabetology alliance

DIABETES IS CLEARLY a cardiovascular disease; vascular events account for between two-thirds and three-quarters of all deaths in type-2 diabetes. Moreover, two out of three patients admitted to the coronary care units, as highlighted in the EUROASPIRE surveys, have either glucose intolerance or overt diabetes.

Cardiologists have, therefore, started to learn a lot more about diabetes, and diabetologists have become more involved in the follow-up of cardiac patients. An important landmark was the ESC/EASD Guidelines launched in 2007 by Professors Lars Ryden and Eberhard Standl. The cardio-diabetology alliance became a useful meeting point for two specialties with a common goal of delivering high quality comprehensive care to this high risk population.

Significant research efforts have helped bring these specialties together. Cardiologists often segregate according to their interest in the lumen or the lining of arteries. 'Luminal cardiology' combines skills with the industry trend, but aspiring researchers often find the endothelium a more challenging area of investigation. And here both cardiologist and diabetologist encounter one of the mysteries of diabetes, the elusive quantum of vascular risk that remains when all other known risk factors have been accounted for. Total cardiometabolic risk arises by virtue of overlap between diabetes, hyperlipidaemia, hypertension, central obesity, and a cluster of other emerging cardiovascular risk factors. And behind all of these appears insulin resistance: cause, consequence, or collateral of 'classic' middle-age spread in our population?

This is why the field is full of myths – and why we are in need of a comprehensive approach and robust alliance to build a new way of understanding and find useful solutions.

After some concerning results of intensified glucose control in patients with type 2 diabetes, and non-inferiority (without superiority) of many new anti-diabetic drugs compared with

placebo, the positive results in survival and cardiovascular and renal outcomes with empagliflozin and liraglutide have been acknowledged with enthusiasm!



Dan Gaita: Cardiometabolic risk needs a comprehensive approach.

'Metabolic healthy obesity'?

Obesity remains the core of the metabolic syndrome. Unfortunately, during the last three decades the worldwide prevalence of obesity has nearly doubled, and mean BMI has increased worldwide by 0.4 kg/m² per decade for men and 0.5 kg/m² per decade for women. However, waist circumference, body composition and other metabolic indicators are now competing with BMI for best defining cardiometabolic risk. One outcome of the first US cardiometabolic think tank was a state-of-the-art review published in *JACC* in 2015 which emphasised that the metabolic syndrome (MetS) should be classified by subtype and stage, which translate to specific evidence-based management algorithms to improve outcomes.

Despite this, no uniform definition of what should be considered 'metabolically healthy' in the obese or overweight

has been established. Investigators often define participants with metabolic healthy obesity (MHO) by the absence of MetS, absence of insulin resistance or, less often, the absence of abdominal adiposity or high cardiorespiratory fitness. But the phenotype of MHO, described by the presence of obesity in the absence of metabolic risk factors, has garnered significant interest. Some studies argue that a specific subgroup of obese individuals is resistant to metabolic complications and recent data from a cross-sectional study support the notion that MHO is accompanied by a more favourable inflammatory status than is metabolically unhealthy obesity.

On the other hand, MHO individuals have a higher all-cause mortality compared with normal weight metabolically healthy individuals. So it is instructive to start with my conclusion from the 2015 ESC Congress debate with Wolfram Doehner – that 'obesity is always bad for cardiovascular disease' – and to reformulate a rhetorical question, as Massimo Piepoli did in his 2016 European guidelines on CVD prevention in clinical practice: 'Does MHO really exist?'

At present the most reliable data come from the long-term results of the Whitehall study that support the notion that MHO is a transient phase moving towards glucometabolic abnormalities rather than a specific 'state'. Thus, maybe more a concept than a real population.

Despite the fact that the simplest questions are the most difficult to answer, from my perspective MHO people will NOT populate the Earth! Good or bad, it's up to you to decide. But please keep in mind that if a man is as old as his arteries, then according to one traditional axiom, add 20 years for diabetes. So I highly recommend you to join today's unique ESC & EASD myth busters Joint Session Symposium.

Cardio-diabetology Alliance: the myth busters
28 Aug 08:30-10:00 Paris - Village 7

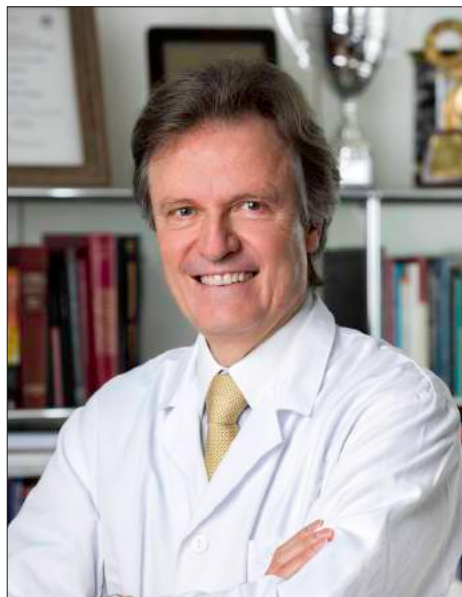
Influence and impact in the European Heart Journal

IN AN ACADEMIC world in which social media plays an ever increasing role, the traditional 'impact factor' may not reflect every aspect of a journal's impact. There will be impact in how often a published paper is cited on Twitter, in science blogs, even in an old fashioned 'news' bulletin. Remember newspapers? So it's worth noting that a study published in the *European Heart Journal* in March this year – on the role of 'positive emotional stress' in Takotsubo syndrome and publicised in an *EHJ* press release as 'happy heart syndrome' – proved the most widely reported paper ever from the journal. Such coverage will not be fully reflected in an impact factor, which is measured only by the number of citations over a limited period.

Nevertheless, the impact factor remains the most accessible measure of journal quality and journal success, and it is a tribute to the ESC journals that three of the top 20 journals in this year's Journal Citation Reports for cardiology were titles from the ESC's stable of journals. The flagship title, the *European Heart Journal*, maintained its 15+ score and rests in third place in the IF league table.

'But impact factor isn't everything,' says Editor-in-Chief Thomas F. Lüscher (pictured above), 'and there are now so many other measures of influence. We had more than 6 million downloads in 2015, which in itself is a remarkable record when you consider there were just 2 million in 2009. It shows that people are reading us, that our papers do have clinical influence.'

Having broken through into the exalted



realm of double-digit impact factors in 2011, the *EHJ*'s latest score represents a consolidated shift of almost five points in just five years. The journal also topped the Journal Citation Report's 'immediacy index', a calculation based on the number of times an article is cited in its year of publication – and thus reflecting speed of citation.

Lüscher attributes such ongoing success to continuing editorial innovation, a quicker time to first decision for all submissions (now down to 14 days), and to a greater global – and not just European – appeal. 'Manuscript submissions from the USA increased by 15% last year,' he says, 'and we have made specific US additions to our list of international associate editors.' Lüscher also

notes increasing appeal in Asia and Australia, with ever stronger relationships in Japan and China. The journal has taken to the road in recent months, with presentations at national society meetings – including those in Japan and China.

Editorial innovations like CardioPulse, which provides a forum for international news and comment, brief communications (a maximum of 1500 words and one figure), podcasts and the 'issue @ a glance' (with associated articles free to view) have proved popular with readers, generating huge numbers of downloads within just a year or two of their introduction.

With around 3500 original manuscripts submitted each year and a rejection rate of 92%, publication in the *EHJ* is never a given. So there will be much interest in a Special Session on Tuesday in which Lüscher, John Jarcho, an associate editor of the *New England Journal of Medicine*, and Rickey Carter, statistics editor of the *EHJ*, will set out their 'criteria for good scientific papers', whose ingredients, says Lüscher, must include clarity, novelty and honesty. There will also be two further Special Sessions reviewing the *EHJ*'s year in cardiology, on prevention and intervention, and on heart failure and valvular disease.

Such clinical influence, of course, lies at the heart of any journal's planning, but there's no doubt that *how* that influence is achieved is now in the throes of great change. 'Yes, we are seeing big changes,' agrees Lüscher. 'We are seeing it in the downloads that

physicians are reading – and their number is going up dramatically. I think this is influence – mentions on Twitter, blogs and other social media. This represents use in everyday practice.' But for the time being at least, the impact factor remains the metric which matters, and right now that too remains a source of pride and satisfaction to the *EHJ*'s editorial team.

What are the editor's criteria for good scientific papers? Meet the editors of the European Heart Journal,
30 Aug 10:10-10:50 Galileo - The Hub

Impact factors of the top ten cardiology journals

J Am Coll Cardiol	17.759
Circulation	17.047
Eur Heart J	15.064
Circ Res	11.551
Nat Rev Cardiol	10.533
JACC-Cardiovasc Imag	7.815
JACC-Cardiovasc Inte	7.63
J Heart Lung Transpl	7.509
JACC-Heart Fail	7.218
Circ-Heart Fail	6.833

Atherosclerosis a target for nanomedicine

OPPORTUNITIES FOR nanomedicine in the management of atherosclerosis will be considered this afternoon in a joint Symposium with the European Atherosclerosis Society.

The prefix 'nano' derives from the Greek for 'dwarf', with nanoparticles defined as small objects behaving as whole units with respect to transport. Similar in scale to biological macromolecules, such as proteins and DNA, nanomolecules, typically in the range of 1-100 nanometres in size, can be engineered to deliver payloads of different drugs in atherosclerosis.

By attaching antibodies, proteins, peptides or other ligands to the surface, a nanoparticle can be targeted to single or multiple receptors on the surface of atherosclerotic plaques. Additionally, neovascularisation, arising from compensatory defence mechanism to restore nutrient supply to the vessel wall, can allow nonspecific targeting of atherosclerosis by nanoparticles.

'The big advantage of packaging drugs into

nanoparticles,' explains Erik Stroes, from the Academic Medical Centre, Amsterdam, 'is that you can deliver high concentrations to the area of interest, enabling efficacy to be increased and side effects reduced.' Thus, using nanoparticles to deliver glucocorticoids in atherosclerosis provides an example of how specific targeting of agents might help patients. Although widely used for anti-inflammatory effect in rheumatoid arthritis, glucocorticoids have not been used in CVD because of their pro-atherogenic effects. Experimental animal models have demonstrated their local administration via PEGylated liposomes has the ability to reduce neo-intimal formation and arterial wall inflammation.

Although 75% of macrophages isolated from the plaques contained liposomes, there was, however, no anti-inflammatory effect. 'We are now in the position where we know we can deliver drugs directly to plaques using nanoparticles,' says Stroes. 'But it appears

inflammation in atherosclerotic plaques may be distinct from classical inflammation. We need to go back to the drawing board and consider if other anti-inflammatory agents might prove a better choice and if we should change delivery systems.'

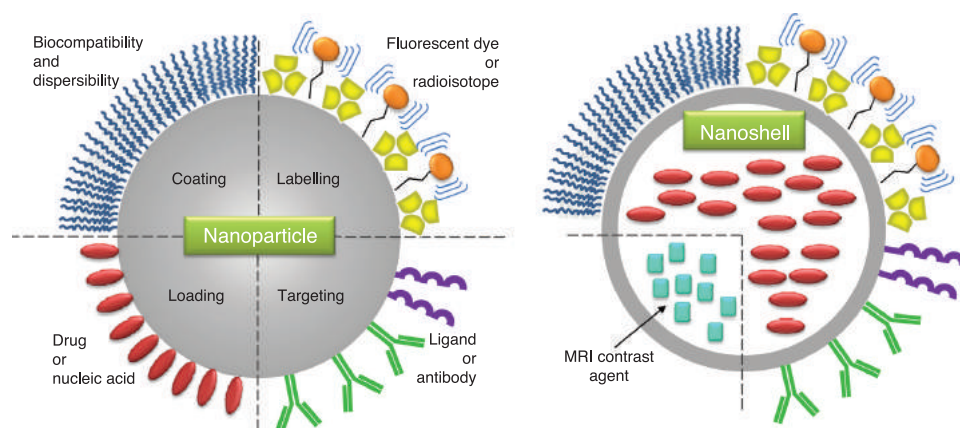
In mouse atherosclerotic models it has been shown that nanoparticles exploiting the inherent targeting properties of HDL can deliver statins. Near infra-red fluorescence images reveal nanoparticle accumulate in plaque-rich regions of the aorta, where they co-localised with macrophages. The investigators showed the arteries of mice given the nanoparticle were 16% more open than arteries in mice with no treatment, and 12% more open than mice given systemic statins.

Use of nanoparticles in cardiology undoubtedly lags behind oncology, where Doxil, a liposomal formulation of doxorubicin, was first approved in 1995 by the FDA. 'The reason for this is that in patients with advanced cancer, high-risk nanoparticulate drugs may be approved as long as they prolong life by a few months,' explains Iwona Cicha from University Hospital, Erlangen, Germany. 'However, many CVD patients live with their conditions for years, which makes the potential toxicity risks posed by nanoparticles unacceptable.' Nanotoxicology, she adds, is emerging as an important area in the field of nanomedicine.

Nanoparticles, says Cicha, can be enormously varied in composition and frequently have multicomponent formulations. In addition to the different types of drugs or contrast agents attached to their surface, antibodies or ligands can be used to achieve specific targeting.



Iwona Cicha: A need to standardise the characterisation of nanoparticle medicines.



In addition to the different types of drugs or contrast agents that can be attached to their surface, nanoparticles can be modified by adding antibodies or ligands for specific targeting. Credit: Eur J Nanomed 2014; 6: 63-87.

The size, shape, surface charge and colloidal stability of nanoparticles can all be modified. Size matters, says Cicha, with nanoparticles smaller than 5 nanometres being quickly cleared by the kidney and those above 100 nanometres rapidly cleared by the liver.

Every parameter you change, says Cicha, can influence circulation half-life, and the biological effects of nanoparticles. 'Right now,' she says, 'nanoparticulate medicines are not treated any differently from other drugs, but regulators must soon realise that their characterisation needs to be standardised. For safety reasons, we all need the reassurance that nanoparticles intended for CV applications have been put through a whole range of defined analytical and toxicity tests.'

Don't miss: Nanomedicine for atherosclerosis
28 August 16:30-18:00 Baku - Village 1

Interpreting findings with non-vitamin K antagonist (VKA) oral anticoagulants in atrial fibrillation – collective views on data from seminal studies to present clinical practice

Find out more at our Satellite Symposium

Join us on Sunday 28 August 2016,
12.45–13.45, Room Prague – Village 9

Moderated by chairs:
Christoph Bode and Jafna Cox



Bayer Satellite Symposium at ESC Congress 2016.
Bayer Pharma AG, June 2016.
L.IT.MKT.06.2016.1478

Signalling modules in cardiac pathophysiology

Denise Hilfiker-Kleiner's theme in today's William Harvey lecture

IN THIS MORNING'S WILLIAM HARVEY lecture on basic science Denise Hilfiker-Kleiner will consider how maternal blood loss at birth has the potential to trigger a deadly sequence of events leading to peripartum cardiomyopathy (PPCM).

Hilfiker-Kleiner, from the University of Hanover, will describe her partnership with the South African cardiologist Karen Sliwa, which has enabled the description of a molecular cascade for PPCM. Their fruitful long-term collaboration, linking basic science, translational research, clinical studies and registries, places the signal transducer and activator of transcription 3 (STAT 3) centre stage, and has led to clinical trials repositioning the old drug bromocriptine to treat this life-threatening condition.

It was while working as a post doc with the late Helmut Drexler that Hilfiker-Kleiner first produced mice with cardiomyocyte restricted STAT-3 deletion, and observed far fewer offspring than anticipated. 'My training as a developmental biologist exploring gender made me go back to look at their mothers,' she recalls. 'To my complete shock, I found many dead in their cages, with the few who survived displaying symptoms of heart failure.'

A serendipitous encounter with Sliwa, from the Hatter Institute for Cardiovascular Research in South Africa, at a cardiology meeting led to the realisation that Sliwa's PPCM patients shared similar characteristics to Hilfiker-Kleiner's female mice, and that they had identified an animal model for PPCM. 'Our example shows how connections made at meetings can really propel your research forward,' says Hilfiker-Kleiner.

Together, she and Sliwa showed that the nursing hormone prolactin plays an important role in PPCM. In the peripartum period they found that STAT-3 protects the maternal heart from excessive oxidative stress, but reduced levels of STAT-3 can result in the enzyme cathepsin D breaking down prolactin. It is the terminal prolactin fragment, 16-KDa Prl, that compromises



Denise Hilfiker-Kleiner, with her colleague Karen Sliwa, went on to show that blocking prolactin with bromocriptine improved outcome in peripartum cardiomyopathy.

cardiac microvasculature and leads to development of heart failure (Cell 2007; 128: 589-600).

The team went on to show that blocking prolactin with bromocriptine rescued the mice, and in a proof of concept pilot that it improved clinical outcomes for 10 women with PPCM (Circulation 2010; 121: 1465-1473). Ironically, their success has led to ethical committees refusing to deny bromocriptine to the

'control' arms of clinical trials, with the result that investigators now have to use registry comparisons for bromocriptine research.

Most recently the team has shown that generating hyperosmolaric test-tube conditions (that simulate blood loss) results in degradation of STAT-3. 'Our latest theory is that high blood loss around the time of birth triggers degradation of STAT-3, and, when combined with the release of prolactin, triggers a deadly sequence of events,' says Hilfiker-Kleiner.

This observation, she adds, is backed by registry data showing that women with low haematocrits are more likely to develop PPCM, and by statistics showing that women in Southern Nigeria have a high incidence of PPCM. 'In Southern Nigeria, where one in 100 new mothers are affected by PPCM, there is a strong tradition to give them salt after the birth and encourage women to lie on heated clay beds,' says Hilfiker-Kleiner, explaining that both these activities encourage dehydration.

In her quest to reduce PPCM, Hilfiker-Kleiner now wants to reach out to obstetricians and general practitioners with her story. 'Maybe simple interventions like giving women who encountered substantial blood loss during delivery saline infusions after birth, and/or iron supplementation could prevent onset of PPCM,' she says.

Moreover, she adds, tests like measuring serum NT-proBNP levels could be introduced routinely to identify women at risk for PPCM, or diagnose it faster.

Don't miss: ESC William Harvey lecture on basic science. Renaissance of signalling modules: the role of STAT3 in the cardiac pathophysiology
28 August 11:50-12:30 Bernini - The Hub

René Laennec lecture on clinical cardiology

With aortic stenosis the most common valvular disease, there are now more diagnostic challenges than ever

IN THE ESC RENÉ LAENNEC Lecture this afternoon Helmut Baumgartner will focus on the current diagnostic and therapeutic challenges posed by aortic stenosis (AS), a field he has been involved in throughout his professional life.

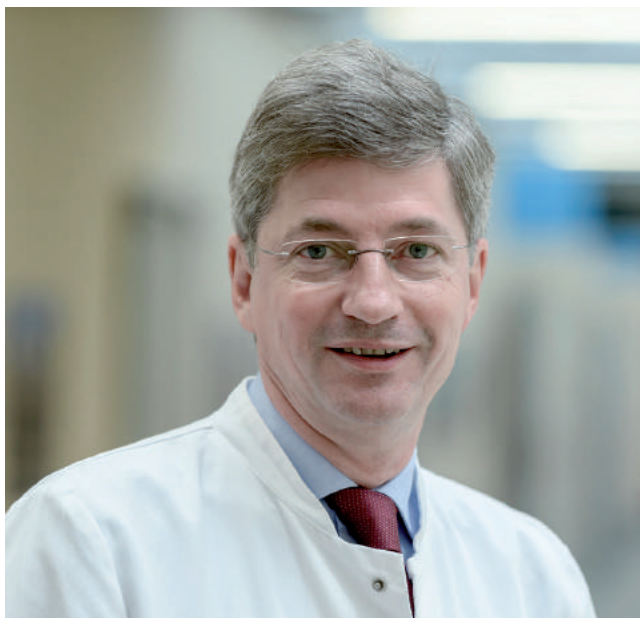
AS, primarily calcific AS, has become the most frequent valvular heart disease in Europe and North America, affecting around 2-7% of people over 65. 'While we've learned a lot about this disease over the years, there are now more open questions regarding diagnosis and treatment than ever before,' explains Baumgartner, from the University of Münster, Germany.

The main diagnostic question for AS during Baumgartner's early career was whether invasive evaluation was required for accurate quantification. Baumgartner contributed to studies identifying sources of error for echo, resulting in echo becoming the gold standard for diagnosis (Cardiology 1990; 77: 101-111; Circulation 1996; 94: 1934-1940; J Am Coll Cardiol 1999; 33: 1655-1661).

The definition of severe AS (mean gradient >40 mmHg and a valve area <1.0 cm²) became well accepted, leading to recognition that patients with poor LVEF and reduced flow may present with low gradients and require dobutamine echo to distinguish between true severe and pseudo severe AS.

More recently, new entities - such as low flow, low gradient AS with preserved EF and normal flow, low gradient AS with preserved EF - have been proposed, although it is still controversial who has severe AS and would benefit from surgery.

'It turned out a problem we described many years ago, which was largely ignored at the time but plays an important role in low gradient AS,' explains Baumgartner. The traditional continuity equation assumes a circular left ventricular outflow tract for the calculation, but extensive use of CT before TAVI has confirmed that most outflow tracts are in fact more or less oval. 'LVOT area is then underestimated, and in consequence flow and valve



Helmut Baumgartner: 'In 2016 deciding between surgery and TAVI has become the major issue.'

area, resulting in misclassification of moderate AS as severe,' Baumgartner explains.

During his time in Gerald Maurer's department at the Medical University of Vienna, Baumgartner and colleagues, made significant contributions to the debate demonstrating that 'watchful waiting' until symptoms occur is safe for asymptomatic patients with severe AS (N Engl J Med 2000; 343: 611-617).

Although later studies questioned this strategy, the reported poor outcomes were largely caused by patients who developed symptoms during follow-up and were not operated on. 'These

studies actually confirmed the safety of 'watchful waiting' and clearly demonstrate that in order to guarantee timely surgery patients must be properly educated and regularly followed,' Baumgartner explains.

He and colleagues demonstrated that the presence of moderate to severe valve calcification together with a rapid increase in aortic jet velocities during follow-up identifies patients with worse outcomes who may benefit from elective surgery and also contributed to defining the role of neurohormones (Circulation 2004; 109: 2302-2308, Circulation 2007; 115: 2848-2855). 'Early detection of interstitial myocardial fibrosis may also be important in risk stratification of asymptomatic severe AS, but requires further research,' says Baumgartner.

Finally, Baumgartner will address choice of AS treatment modalities. 'At the beginning of my career the main question was when to use biological and when to use mechanical valves. But in 2016 deciding between surgery and TAVI has become the major issue,' he says. While the role of TAVI has become evident in elderly patients with increased surgical risks, it is still limited in younger patients. 'Younger patients can have different valvular anatomy with an increased likelihood of the congenital abnormality of a bicuspid aortic valve that could impact their results,' says Baumgartner. Additionally, trials show higher numbers of patients require permanent pacemakers for atrioventricular block to be fitted after the TAVI procedure than those undergoing surgery. 'Pacemakers can have long term complications making their use far from ideal in younger patients who have longer life expectancies,' says Baumgartner.

Don't miss: ESC Rene Laennec lecture on clinical cardiology.
28 August 14:50-15:30 Bernini - The Hub

More on exercise: every little helps

Protective effect found ‘dose-dependent’ in older subjects

EVEN MODERATE leisure-time physical activity can have cardiovascular health benefits, according to a study presented at a press conference yesterday by researchers from Oulu, Finland. Their 12-year study in nearly 2500 adults aged 65 to 74 years found that moderate physical activity - defined as walking, cycling or other forms of light exercise (fishing, gardening, hunting) at least four hours per week - reduced the risk of an acute cardiovascular event by more than 30%. High levels of physical activity - running, jogging, skiing, gymnastics, swimming, ball games, heavy gardening or sports competitions at least three hours a week - led to even greater risk reductions.

‘The role of physical activity in preventing cardiovascular disease in people of working age is well established,’ said Professor Riitta Antikainen. ‘But relatively little is known about the effect of regular physical activity on CVD risk in older people.’

Baseline data included self-administered questionnaires on physical activity and other health related behaviour, clinical measurements (blood pressure, weight and height), and laboratory measurements including serum cholesterol, with participants followed up to the end of 2013. Deaths and incident CVD events were collected from national registries.

Results showed that moderate and high leisure time physical activity were associated with a 31% and 45% reduced risk of an acute



Riitta Antikainen: Cardiovascular benefits for the elderly from even moderate exercise.

CVD event, and 54% and 66% reduction in CVD mortality.

‘Our study provides further evidence that older adults who are physically active have a lower risk of coronary heart disease, stroke, and death from cardiovascular disease,’ said Antikainen. ‘The protective effect is dose dependent – the more you do, the better.’

While this study emphasised the importance of exercise to older people, a study from Brazil shows just what can be done to prevent obesity in children. ‘Healthy School, Happy School’ was a randomised controlled trial designed to test the effectiveness of an intervention to halt an obesity trend in children. It was conducted in Feliz, Brazil, by nutritionists in the Research Group on Cardiovascular

Prevention in Childhood and Adolescence.

‘Feliz is the Portuguese word for “Happy”, and the study name pays tribute to this small but very special town in South Brazil,’ said investigator Daniela Schneid Schuh. ‘Feliz has one of the highest human development indexes in the country. But health problems such as obesity, hypertension and other chronic diseases are aggravated by rising urbanisation and changing eating habits.’

Four schools were randomly assigned to one of two groups for nine months: the intervention group (two schools with 73 children), which focused on lifestyle changes at school and at home, or the control group (two schools with 140 children), which only received the usual recommendations from the regular school curriculum.

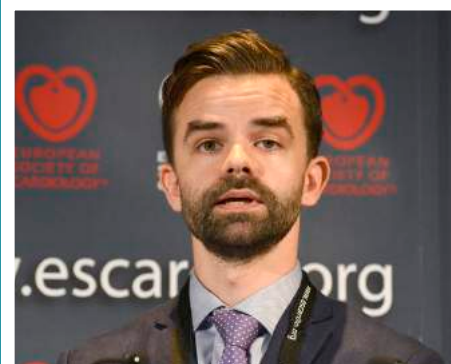
Intervention activities occurred monthly in the schools’ multimedia room or sports court, with seminars and workshops about physical activities, healthy eating and bullying. This last topic was included after talking to children, who reported dissatisfaction with body image and suffering bullying from classmates for being obese.

The children in the control group showed a significant increase in BMI after the nine months of the study, while BMI in the intervention group remained as before. ‘Being able to increase physical activity and better eating in childhood may be crucial for building a healthy and happy life in the long run,’ said Schuh.

Time to include socio-economic status in CVD risk assessment?

‘Are you rich or poor?’ asked researcher Joel Ohm from the Karolinska Institute in Stockholm. ‘Married or divorced?’ For both might affect your risk of a second heart attack or stroke. His study in nearly 30,000 patients with a prior heart attack found that the risk of a second event was 36% lower for those in the highest income quintile than in the lowest and increased by 14% in divorced compared to married patients.

Ohm said: ‘Our study shows that in the years following a first MI, men and women with low socioeconomic status have a higher risk of another heart attack or stroke. This is a new finding and suggests that socioeconomic status should be included in risk assessment for secondary prevention. Simple questions about other socioeconomic variables such as marital status and educational level could make a difference.’



Joel Ohm: Income mattered in a large secondary prevention study.



This programme is accredited by the European Board for Accreditation in Cardiology (EBAC) for 2 hours of external CME credit. Each participant should claim only those hours of credit that have actually been spent in the educational activity.

Organised by: University Hospital of Umeå, Sweden
Course Director: Ulf Näslund, Professor of Cardiology



EBAC ACCREDITED EDUCATIONAL PROGRAMME HELD DURING THE ESC CONGRESS 2016

The clinical journey after an acute coronary syndrome: strategies for optimising antiplatelet therapy

EXPERTS ON THE SPOT

Sunday 28th August | 10.15 – 10.45 | Bernini, The Hub

CHAIRPERSONS SPEAKER

Stefan James | Sweden Marc Bonaca | US
Gabriel Steg | France

This EBAC Accredited “Experts on the Spot” session follows on from the Educational Programme session on Saturday 27th August 2016 | 15.30 – 17.00. Participants attending both sessions will be entitled to receive 2 CME credits.

Supported by an unrestricted educational grant from AstraZeneca

In compliance with EBAC/EACCME guidelines, all speakers/chairpersons participating in this programme have disclosed or indicated potential conflicts of interest which might cause a bias in the presentations. The Organising Committee/Course Director is responsible for ensuring that all potential conflicts of interest relevant to the event are declared to the audience prior to the CME activities.



Pope Francis at ESC

Preparations for an historic visit

As previously announced, the Pope will be visiting us at the end of ESC Congress on Wednesday 31 August. This will be an historic event and a unique opportunity for you and our fellow delegates to participate.

As you can imagine, there are a number of security requirements with the visit of a Head of State, so we would like to request your co-operation if you are planning to participate in the visit at the Congress on that final day.

More information will be provided by email, on our mobile app and in *Congress News* nearer the time, but the main points we are able to confirm now are:

- All delegates will go through an

airport style security check on arrival at Fiera Roma on Wednesday. Please allow plenty of extra time to complete this security check that morning. Delegates carrying suitcases will need to clear security before leaving their bags at the cloakroom, which is located before the main entrance arch.

- All delegates will need to arrive at Fiera Roma before 11:00 on Wednesday. After that time, entrance to the Fiera Roma will not be possible until after the Pope's visit. If any of your colleagues are planning to register for a Congress day pass on that day, they will need to register before 11:00.

- The ESC Clinical Practice Guidelines Highlights session will start at 08:30 and the Congress Highlights Session will start at 09:45. There are no other changes to the programme planned on Wednesday morning.

- After the Congress Highlights Session ends at 11:45, delegates will be shown by ESC staff to the relevant area of the Fiera Roma where you will be able to see the Pope. We expect the Pope to arrive at 12:15 and for the visit to be completed within one hour.

We will continue to keep you informed as we approach the visit on Wednesday, which we hope will be an historic ending to this year's ESC Congress.



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Your view of lower BP targets?



Eduardo Algeria Ezquerra, clinical cardiologist from San Sebastian, Spain

The reality of my clinical practice is that most of my hypertensive patients are elderly. While lowering blood pressure as much as possible may be effective in terms of increasing life expectancy, in real life practice it can be very difficult to achieve values under 120 mmHg. The problem for older patients is that these really low levels induce side effects, such as electrolyte abnormalities and kidney problems, and put them at greater risk of suffering from falls, which can lead to other serious pathologies. To my mind, there are only marginal gains to be made for older patients in living longer and many prefer to achieve better quality of life.

faces in the crowd



Gabrielle Schiattarella, molecular cardiologist from Dallas, Texas.

‘While the SPRINT trial, which suggested that systolic blood pressures of 120 mmHg are beneficial, represents a real breakthrough in hypertension therapy, I feel that the biggest overall health gains can be made in helping more patients to achieve guideline blood pressure levels of 140 mmHg. I think that the current drug armamentarium will be sufficient to achieve levels of 120 mmHg if patients are encouraged to take more exercise and eat better diets. We still don't know how low we can go, and in future trials we'll be comparing systolic pressures of 120 mmHg with 110 and even 100 mmHg.’

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Lecture Room Brussels – Village 8
Sunday, August 28, 2016
18.30-19.30

Satellite symposium

Going further in treatment of angina with ivabradine

Chairpersons:

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(Italy)

J.-C. Tardif
(Canada)

Speakers:

R. Ferrari (Italy)
S. Gloekler (Switzerland)
G. Heusch (Germany)
A. Lyon (UK)

G. Montalescot (France)
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