THE PONTIFICAL ACADEMY OF SCIENCES

Working Group on

Atherosclerosis:
the 21st Century Epidemic

31 May – 1 June 2010 • Casina Pio IV

VATICAN CITY 2010

In carrying out its distinctive service, the Pontifical Academy of Sciences always relies on the data coming from science and the Magisterium of the Church. In particular, concerning the present study group [on *The Signs of Death*], Christian Revelation also invites the man of our times, who in many ways seeks the real profound meaning of his existence, to face the theme of death casting his eye beyond human reality in its purest form and opening his mind to the mystery of God. **Indeed, it is in the light of God that the human creature better understands himself and his final destiny, the value and meaning of his life, a precious and irreplaceable gift of the almighty Creator.**

Benedict XVI, Letter dated 8 September 2006 to his venerated Brother H.E. Msgr. Marcelo Sánchez Sorondo, Chancellor of the Pontifical Academy of Sciences, concerning the working group on *The Signs of Death*, 11-12 September 2006.

INTRODUCTION

H.E. Msgr. Marcelo Sánchez Sorondo, Chancellor
The Pontifical Academy of Sciences

The Pontifical Academy of Sciences, whose purpose is to promote the progress of the sciences for the common good of the human person, in its Study Week of 31 May – 1 June 2010 at its headquarters in the Vatican, would like to focus on the wellbeing of the vascular system, taking into account the revolutionary contributions of the last century in relation to the human heart and brain.

Vascular Disease accounts for 15 million deaths per year worldwide. This represents 30% of all causes of mortality. Most vascular deaths are secondary to brain and heart infarctions. Stroke (cerebrovascular disease) ranks as 1st, 2nd and 3rd cause of death depending on the country or world region. Public recognition of cerebrovascular disease lags significantly behind identification of coronary artery disease.

Risk factors for Vascular Disease: known and treatable…

Genetic predisposition, hypertension, diabetes, cholesterol, smoking, lack of exercise and obesity are the main risk factors that predispose to the occurrence and progression of atherosclerosis.

Increased blood pressure causes heart, brain and kidney disease and accounts for 13% of all deaths worldwide. Hypertension is easily identified and treatable, yet only 2 out of 3 patients are diagnosed and up to 80% of those diagnosed are treated but do not reach target blood pressure goals. Hypertension accounts for 54% of stroke and 47% of coronary heart disease deaths. With 1 billion people affected, the prevalence of hypertension is increasing worldwide. Against deeply rooted medical traditions, recent data has shown that patients older than 80 years also benefit significantly from strict blood pressure management.

Actively screening and treating hypertension, cholesterol and diabetes are justified since more than 50% of vascular deaths are due to few risk factors. Moreover, different studies have shown that coronary heart disease and stroke share the same risk factors. Importantly, the most important vascular risk factor is a previously suffered vascular event. This emphasizes the importance of stringent medical treatment of conventional and other vascular risk factors once a cardiac, cerebral or other vascular event has occurred. Data from the Framingham study has shown that, counter intuitively, most vascular events occur in people with a moderate load of vascular risk factors.

How is Vascular Disease distributed throughout the world?

In low income countries, vascular disease accounts for 80% of all deaths (11 million per year). In these regions, cardiovascular disease occurs 1 to 2 decades earlier compared to developed countries. Sadly, because of a high case fatality rate, prevalence of cardiac and cerebrovascular disease in developing areas is lower compared to the developed world.

Epidemiological studies from developing regions are scarce and often of limited reliability. Good epidemiology studies are costly, complex and demanding and resources in developing countries are limited. The details on the distribution and characteristics of Vascular Disease in the developing world are needed to identify the areas in greater need to distribute resources accordingly. Surveillance data helps countries to develop, implement and monitor prevention programs.

If Governments do not include health policy changes in their agendas, in the next five years non communicable vascular diseases will overcome infectious diseases (TB, HIV and malaria) as the number one cause of death in countries such as India and China. In the latter, there are about 300 million smokers, 160 million hypertensive people and 20% obese children between 7 and 17 years of age, something unknown to this region in the past.

Cognitive decline: a major health burden caused by Vascular Disease

Dementia poses a large burden of disease worldwide. Cerebral vascular injury causes cognitive impairment and dementia with a frequency similar to degenerative dementia. For a given load of neuropathology findings of Alzheimer's disease, the presence of cerebrovascular disease correlates with earlier clinical manifestations. Some authors have speculated and provided data to support that hypertension results in decreased cerebral blood flow in brain structures commonly affected by Alzheimer's disease predisposing a vulnerable state for the development of degenerative dementia. Increased blood pressure and cholesterol in the 4th and 5th decades of life correlate with dementia onset in the 7th decade.

There is a major 'implementation' problem by which the known measures and medications to prevent vascular disease are largely under-used

Prevention is the first step in the cure for Vascular Disease. Yet, there is a major gap between knowledge and the implementation of measures for primary as well as secondary vascular disease prevention. Effective treatments for the acute and chronic phases of coronary and cerebrovascular disease are largely underused. The scientific community and Governments through their Ministries of Health are responsible for the effective implementation of policies that achieve lower smoking rates, increased physical activity, healthy eating habits, and high detection rates for hypertension, diabetes, abnormal lipids and other vascular risk factors. Stroke Units, proven effective by scientific evidence, should be available in most clinics/hospitals with Coronary Units.

There is no doubt that significantly more interest is devoted to acute and invasive techniques compared to prevention. And it is paradoxical that patients have artificial heart valves inserted with endovascular techniques and cerebral clots removed with cork-screw like devices, among other novel techniques, but various studies have shown that patients are frequently discharged from hospitals following a vascular event without the adequate dose of anti-thrombotic, anti-hypertensive or cholesterol lowering medications. However, a measure as simple as counseling during hospitalization has been proven to increase adherence to treatment after discharge from the Hospital. The general public and physicians need to be educated on the importance of vascular disease prevention. This teaching takes time but it is most effective when it starts as early as childhood. Healthy young adults must understand that a vast majority have vascular risk factors that justify treatment in the asymptomatic stage.

The challenge: Effective Prevention of Vascular Disease

The knowledge on vascular disease that has accumulated over the last decade is greater than that gained in the entire previous century. Commitment with vascular disease prevention has resulted in a 70% death reduction in the USA, Canada, Australia and the UK. Primary prevention provides an invaluable opportunity for early intervention. Unfortunately, data shows that the people at highest risk have the lowest knowledge about vascular disease. In one study following an education campaign in the year 2000, respondents could only name one warning sign of stroke. In one survey in India, close to 50% of respondents did not know that the brain is the affected organ in stroke. In countries from Africa and Latin America, up to 50% of patients go to alternate medical healers before consulting in a Hospital. As an example, only 50% of people diagnosed with atrial fibrillation receive anticoagulants and just 1% of patients are treated among those who are candidates to receive thrombolytic therapy in the first few hours after occlusion of a cerebral vessel.

The pharmaceutical industry is a major player in the vascular disease battle. Many subsets of the world's population could benefit from a 'polypill' simultaneously targeting various vascular risk factors. Among the important achievements to be expected in this sector is the production of affordable medications through the conduction of affordable trials. Large amounts of money are invested by the pharmaceutical industry and biotechnology companies in research and development of new therapeutic molecules. The scientific community should increase the interaction with the industry and influence the research lines likely to have a novel and higher therapeutic yield.

Conclusions

If the vascular disease burden could be reduced 2% per year, 36 million untimely deaths could be avoided by the year 2015. The World Health Organization has provided data showing that 80% of cardiac events and strokes could be reduced with diet, physical activity and smoking cessation. There is also data proving that 80% of stroke risk would be reduced with adherence to practice guidelines. A wealth of studies has proven the effectiveness of cardiac and stroke units. Yet, with the exception of a few developed countries heading in this direction, results in most world regions drift far from these projections.

In summary, preventive measures that should begin during childhood are needed to educate individuals on how to avoid the most common risks of vascular disease. In addition to the former, disease specific information should be provided to the population as a whole. Behavioral changes at the community level could be expected following effective education and information programs. Active Government participation and commitment with the appropriate health policies are a sine-qua-non to achieve these goals. The Health System, Unions, and other health players should understand the social and financial benefits of vascular disease screening and prevention programs.

Vascular Disease is the field of interest for Cardiologists, Vascular Neurologists, Diabetes, Lipid, Genetics and Nutrition experts, Epidemiologists, Vascular Surgeons, and Endovascular specialists. They all have an increasingly larger number of specialty meetings and seldom participate in strongly integrated conferences. Pulling the rope in the same direction will surely increase the yield in the battle against Vascular Disease. A closer cooperation among the different vascular specialties should be encouraged and the integrated meeting of most vascular disciplines at the Pontifical Academy of Sciences, is a significant contribution to this endeavor.

The moral imperative of our meeting is to make people and private and public institutions, at the national and international level, aware, as was done in the case of alcoholism, drug addiction and smoking, that most risk factors are either under treated or simply not treated, and convince them to adopt adequate precautions in order to avoid premature death or survival with physical and/or mental impairments.

Monday, 31 May 2010

8:30	*Introduction and Welcome*
	World Health Organization: EPIDEMIOLOGY
9:00	*Epidemiology, Global Public Health; The Need for Equitable Action to Address Cardiovascular Disease* **Shanti Mendis**
	DIABETES and OBESITY
9:45	*The Importance of Diet, Obesity and Type II Diabetes for Vascular Disease* **Arne Astrup**
	HYPERTENSION
10:30	*Hypertension: So Much Published, So Little Accomplished* **Conrado Estol**
11:15	Coffee break
	LIPIDS
11:45	*Lipids: HDL, LDL, Role in Primary Prevention, the Message from Trials?* **Terje R. Pedersen**
	RESEARCH NIH
12:30	*Vascular Disease: Ongoing National Institute of Health Research & Resources* **Walter Koroshetz**
13:15	Lunch at the Casina Pio IV
	HEART DISEASE
15:00	*Acute Myocardial Infarction: A Century of Progress and a Look into the Future* **Eugene Braunwald**
15:45	*Genetic and Environmental Factors for Ischaemic Heart Disease* **Attilio Maseri**
16:30	Coffee break
17:00	*The Heart and the Brain: AF, CHF, PFO, the Aorta* **Pierre Amarenco**
17:45	*Surgical Options in Myocardial Insufficiency* **Felix Unger**
18:30	*Cardiovascular Disease: From Treatment to Promoting Health; A Challenge for the Next Decade* **Valentin Fuster**
19:15	General Discussion
20:15	Dinner at the Casina Pio IV

Tuesday, 1 June 2010

CEREBROVASCULAR DISEASE	
8:00	Guided tour of the Vatican Museums, including the Sistine Chapel
9:00	*Acute Stroke Treatment: A Window of Opportunity* **Werner Hacke**
9:45	*Cerebrovascular Frustrations: Cerebral Hemorrhage and Neuroprotectants* **Allan Ropper**
10:30	*Stroke: Antiplatelets, Anticoagulants and the New Medical Strategies* **Geoffrey Donnan**
11:15	Coffee break
11:45	*Vascular Cognitive Impairment: Concept, Epidemiology and the Effect of Risk Factors. Relation to Alzheimer's Disease* **John O'Brien**
12:30	*Cerebrovascular Disease: Lessons from the Past for the Near Future* **Louis R. Caplan**
13:15	Lunch at the Casina Pio IV
14:15	Round Tables • **Top 5 priorities for the next 5 years** (10 minutes each participant) • **Focus on:** **Education/Cultural** **Health Politics** **Medical Goals: Polypill** **Low Income/High Income Countries**
18:00	Departure from the Casina Pio IV by bus to attend the concert at Prince Boncompagni's residence at Villa Aurora (via Lombardia 42)
19:00	Private concert of baroque music offered to the participants by Prince Boncompagni at his residence, followed by dinner and viewing of his unique art collection
22:00	Bus leaves Prince Boncompagni's residence to take participants back to their hotels

Wednesday, 2 June 2010

CEREBROVASCULAR DISEASE	
9:30	*General Audience with the Holy Father. Open to all Participants.*

Vascular Disease: Ongoing National Institute of Health Research & Resources

Walter Koroshetz

The National Institutes of Health (NIH) is the primary US agency for conducting and supporting medical research. Through the support of the American people the NIH annually invests over 28 billion in medical research. More than 83% of the funding is awarded through an open, competitive process to more than 325,000 researchers at over 3000 universities and other research institutions. The NIH funds most of the basic biological research in the US and it's main focus has been on empowering scientists to make the discoveries that will improve health. It also funds "translational research" aimed at turning scientific discoveries into better therapeutic or diagnostic products. Large expensive clinical trials are also funded by NIH to determine whether new treatments are efficacious. Comparative effectiveness research is a longstanding part of the NIH sponsored programs though there is increased emphasis recently to redouble efforts in this area to inform US health care reform. Among its achievements the NIH lists the fall in death rates from heart disease and stroke which fell by 40% and 51% respectively between 1975 and 2000.

The NIH is composed of 27 institutes and centers. The bulk of research in cardiovascular disease is funded by the National Heart Lung and Blood Institute (NHLBI). The bulk of research in stroke is funded by the National Institute of Neurological Disorders and Stroke (NINDS). The two institutes work together on a variety of large prevention and epidemiologic projects. Vascular disease research related to diabetes and obesity is also of interest to the National Institute of Diabetes, Digestive and Kidney disorders. Vascular disease affecting vision is funded by the National Eye Institute. The Fogarty International Center at the NIH focuses on advancing global health. It develops grant programs that are funded by the different NIH Institutes. The NHLBI and the National Institute for autoimmunity, infectious disease (NIAID) and the National Cancer Institute have substantial international research efforts underway around the globe. The NHLBI has set up 11 Centers of Excellence to combat chronic disease in developing countries (Guatemala, Peru, Tunisia, Kenya, South Africa, India, Bangladesh, China, South Africa). The new NIH Director, Dr. Francis Collins has made an enhanced NIH contribution to global health one of his 5 major themes.

Major ongoing research areas in cardio and cerebrovascular disease include:

1) A large study (SPRINT) of over 7500 persons to determine whether aggressive blood pressure lowering reduces stroke, renal failure and heart disease.
2) A large epidemiological study (Regards) in 30,000 people to understand why African Americans have higher stroke mortality than Caucasians.
3) A large study to determine whether patient outcomes are improved by tailoring warfarin dosage (an anticoagulant) based on gene polymorphisms that affect drug metabolism.
4) Multiple studies to determine the association between risk factors, vascular disease and cognitive impairment in the elderly (ARIC, SPRINT-MIND).
5) Studies of which medications are best to prevent second small vessel stroke, stroke after transient ischemic attack, and stroke in persons with heart failure.
6) Relationship of obesity to vascular disease.
7) Multi-ethnic studies of atherosclerosis (MESA) involving over 6000 men and women in US.
8) The Center for Disease Control and Prevention (CDC) is another agency in the US Department of Health which is expert at surveillance studies such as the National Health and Nutrition Examination survey which combines interviews and physical examinations.

The greatest health impact in fighting the burden of cerebro- and cardiovascular disease can be made by wide dissemination of treatments for those risk factors already established by high quality research. Hypertension is by far the greatest modifiable risk factor. Decreasing tobacco use, obesity, sedentary lifestyle, and the treatment of atherosclerosis by lipid lowering agents and anti-platelet agents are relatively simple measures that research suggests could save millions of lives.

Cerebral Hemorrhage and Neuroprotection

Allan H. Ropper

Despite the advances in understanding and treatment of cerebral vascular disease, two areas stand out as lagging behind. First, all attempts to ameliorate the effects of intracerebral hemorrhage have met with disappointment. In particular, after numerous uncontrolled or poorly controlled case series, the STICH trial has settled, within limits, that surgical removal of clots does not improve outcome. This counterintuitive result will continue to be re-examined and the trial may have inadvertently legitimized removal of hemorrhages that are small and close to the cortical surface.

These disappointing results point to an incomplete understanding of the effects of a rapidly expanding blood clot on the adjacent brain, both in the acute and subacute phases. For example, studies conflict regarding an increase or decrease in cerebral blood flow in the tissue adjacent to a cerebral hemorrhage. The effects on intracranial pressure are also variable, further suggesting that we lack some elemental understanding. Decisions regarding blood pressure control after hemorrhage are made on very tentative presumptions abut autoregulation and ICP. Removal of the clot still may make sense to lower ICP, despite STITCH but how

to incorporate this into clinical practice is unclear. Second, a putative benefit of corticosteroids has never been proven and may be partly been negated by the CRASH trial in head injury.

In the field of neuroprotection, almost no progress has been made despite enormous academic and industry investment. Here again, very basic assumptions may be flawed such as the apoptotic mechanism of ischemic neuronal cell death and its potential for amelioration. Targeting free radical production, maintenance of membrane stability, and neurotoxic effects of released neurotransmitters, have so far failed. An object lesson in this disappointing area has been NXY-059, a free radical trapper that was highly promising in experimental models of stroke and an initial clinical trial but failed in SAINT-2. Aside from the differences between animal and human circumstances of ischemic cerebrovascular disease, it may be that endothelial cell and astrocytic damage is not being addressed. The most persuasive pathobiological experiments of 40 years ago that detailed the "no reflow phenomenon" (described by Adelbert Ames) have not been taken into account.

In contrast, the success of hypothermia after VT cardiac arrest suggests that a broader view of cell preservation might be taken. One of the most curious aspects of recent medical sociology has been the lack of adoption of hypothermic protocols after arrest. One public service advance might be to raise public and physician awareness of the need to institute hypothermia in the field after arrest and continue it under close monitoring in order to improve neurologic outcomes for this segment of the population.

Acute Myocardial Infarction: A Century of Progress and a Look into the Future

Eugene Braunwald

Acute myocardial infarction (AMI) as a pathological-clinical entity that was first described in 1909 by two Ukrainian physicians, Obratsov and Strazhesko. Soon thereafter, AMI became recognized with increasing frequency and by the middle of the twentieth century it was established as the most frequent cause of death in the industrialized countries. AMI seemed to occur most frequently in middle-aged men at the height of their productive lives and when they had their greatest family responsibilities. It usually occurred suddenly and without any warning and was likened to a "bolt out of the blue".

In 1950, approximately 25% of patients died suddenly before they could arrive in a hospital. Treatment was symptomatic and was directed principally to the relief of the pain which was often severe. About 30% of patients with AMI admitted to the hospital died within 30 days – approximately one half succumbed to a fatal arrhythmia and the remainder died because of failure of the cardiac pump. Another 25% of survivors who were discharged from the hospital died within one year – most commonly from failure of the cardiac pump.

Since 1950, several important advances have occurred:

1) It is now recognized that AMI is usually secondary to coronary atherosclerosis and occurs most often in patients with predisposing (risk) factors such as smoking, diabetes, elevated serum cholesterol concentrations and hypertension. This has led to measures to reduce risk factors and these have been successful in lowering the incidence of AMI.
2) Arrhythmic deaths were prevented by the development of the coronary care unit, in which cardiac resuscitation, including ventricular defibrillation, can be carried out; this development immediately reduced AMI hospital mortality by half.
3) Next, efforts were made to reduce the extent of myocardial necrosis. This has been accomplished by reperfusion of the threatened ischemic myocardium. Reperfusion was carried out first, by lysing the offending clot (fibrinolysis), then by balloon angioplasty (PTCA) and in the last 15 years by stenting the occluded artery. These efforts have reduced 30 day mortality to approximately 7-10%.
4) Heart failure post myocardial infarction has been prevented or treated successfully by inhibitors of the renin-angiotensin system. This has reduced the late (post-hospital discharge) mortality by one third.

Despite these impressive accomplishments, total mortality secondary to AMI remains high, especially in the elderly (>75 years). Several approaches are now under consideration:

1) Commencing aggressive primary prevention earlier in life, i.e. in the thirties or forties in patients with coronary risk factors;
2) Development of drugs which increase high density lipoproteins;
3) Treating patients with acute pump failure with assisted circulation and simultaneously obtaining their own bone marrow cells that are then cultured in vitro and reinjected. Once these cells have restored the damaged heart's pumping action, the assisted circulation can be discontinued.

Hypertension: the Gap Between Knowledge and Achievements

Conrado J. Estol

There are more than 1 billion hypertensive patients worldwide. More than 7 million deaths (13% of the world's total) occur annually secondary to the effects of hypertension. The life time risk for one person to develop hypertension is close to 90%. Hypertension accounts for more than half of strokes and almost half of myocardial infarctions amply surpassing other known risk factors. In fact, as a risk factor for stroke, hypertension is only second to having suffered a stroke and equal to atrial fibrillation. These facts make hypertension the most important of treatable vascular risk factors. Available data from a myriad of randomized clinical trials testing different hypertension treatments in both the cardiology and stroke arenas have shown a significant reduction in vascular endpoints for treated patients. Even control

of slight hypertension significantly reduces the risk of cardiovascular events.

However, and despite the wealth of evidence showing the negative effects of untreated hypertension, most patients are either not diagnosed or diagnosed and uncontrolled. A number of reasons could explain why.

First, a valid question is: What is "normal" blood pressure? The VII Joint Committee to address the issue defined 130/80 mmHg as the threshold value splitting normal from abnormal blood pressure. However, blood pressure is a continuous vascular risk variable and this means that each value, to a certain point, correlates with an increased vascular risk. Recent meta-analysis which have evaluated more than 1 million people with anti-hypertensive treatment, have shown that the benefit of blood pressure reduction is observed down to values of 115/75 mmHg. The benefit with anti-hypertensive treatment was observed irrespective of previous blood pressure and of history of cardiovascular disease. The NIH will soon be launching SPRINT, an important randomized clinical trial to be conducted in the US to evaluate the benefit of maintaining a systolic blood pressure lower than 120 mmHg. In summary, current values used as "normal" may be higher than those needed to prevent vascular damage.

Secondly, there are a number of strongly rooted myths that contribute to the poor results in blood pressure control. It has long been accepted that a higher blood pressure is normal in elderly people. The HYVET study included almost 4000 patients older than 80 years of age and showed that those treated with a goal of 140/80 mmHg had a significant reduction in all vascular endpoints, in the incidence of side effects and, unexpectedly, in death from "any cause". Another difficult barrier has been the concept of "white coat hypertension" introduced after observing patients that had normal blood pressure at home and increased values at the physician's office. This apparently "benign" condition is strongly questioned by a large number of well design studies that have shown a correlation between "white coat" hypertension and increased carotid plaque and carotid intima-media thickness, left ventricular hypertrophy, MI, sudden death and many other vascular disease markers. Most important, an Australian study has shown that the differences between blood pressure measured at the office and at home are never greater than a few millimeters of mercury. This implies that when pressures are moderately or significantly elevated at the office they should also be abnormal in home measurements. We are now evaluating 20.000 patients that had blood pressure evaluations at the office and were also instructed to report a self-measured blood pressure 1 week after the first office measurement and 3 weeks before the second office determination. Results show that the values reported by patients are significantly lower than those measured at both clinic visits and, more concerning; the proportion of normal blood pressure values was significantly greater when self reported (i.e. false negatives).

Finally, in one study published a few years ago we determined, in line with observations from other groups, that most patients evaluated at a Neurology Clinic were hypertensive and either not previously diagnosed or diagnosed and uncontrolled. They were all referred to their primary MD or to a cardiologist for evaluation and treatment. However, a point of concern was that from the 85% that returned for follow-up to our clinic, 90% were still hypertensive and nothing had been done by their evaluating MD's. In a new study on 1500 patients we observed the same rates of undiagnosed and diagnosed but uncontrolled hypertension but this time we treated patients achieving a 40% control rate.

Blood pressure is easily measurable and hypertension is easily treatable. Yet, there is a major problem with knowledge "implementation" and blood pressure control. The public and the medical community need education about the importance of hypertension control. Consensus on the "normal" value is needed and efforts have to be placed in achieving the defined target. Blood pressure measurement techniques should be unified, myths have to be eliminated and an internationally developed guideline needs to be published.

Lipids: HDL, LDL, Role in Primary Prevention, the Message from Trials?

Terje R. Pedersen

Epidemiological data demonstrate that blood lipoprotein levels are the strongest determinants of risk of cardiovascular disease. Randomized clinical trials have provided overwhelming and conclusive evidence that reduction in low-density lipoprotein (LDL) cholesterol blood levels proportionately reduce the risk of cardiovascular disease. The risk reduction can be observed in almost all populations that have been studied, including the elderly and those with relatively low cholesterol levels. The relative risk reductions per unit reduction in LDL cholesterol is essentially the same in all populations, with possible exception of those at the highest age, indicating that the mechanism of benefit is the same in secondary and primary preventive situations. Statins are by far the most widely used class of drugs to reduce risk and have been shown to be safe with few and rare adverse effects. Simvastatin and pravastatin, two of the most popular statins, have lost patent rights and have become available as cheap generic drugs, and atorvastatin is about to loose patent rights soon. The budgets of health care providers determined for preventive clinical results measures will therefore allow much greater proportions of the public to benefit from the advantages of statin use. In China and other Asian countries extracts from red yeast rice containing lovastatin have been used widely for centuries and such products have been shown to reduce coronary morbidity and mortality as well. Surveys have shown that physicians do not readily adopt the message from clinical trials that intensive lipid intervention with drugs is necessary to achieve optimal results in secondary prevention for middle aged or elderly individuals. In primary prevention the intensity of statin treatment among high risk individuals is prob-

ably less important than the timing of start of intervention. Strategies to increase high density lipoprotein (HDL) levels have so far largely failed to provide convincing evidence of benefit. Some drugs that increase HDL-cholesterol modestly also modify other lipoproteins and the specific effect on clinical results from the increase of HDL has been difficult to separate from the other changes in lipids. Studies are under way that might shed more light on this aspect of lipid intervention. The lecture will deal with the present state of lipid intervention and discuss the implications for long-term strategies of regulatory authorities in disease prevention.

Epidemiology, Global Public Health; The Need for Equitable Action to Address Cardiovascular Disease

Shanthi Mendis

Cardiovascular diseases (CVD) are responsible for nearly 50% (17.1 million) of deaths due to noncommunicable diseases (NCDs). Almost 80% of the CVD burden is in low and middle income countries. Cardiovascular diseases once associated with abundance are now heavily concentrated in poor and disadvantaged groups.

Powerful global forces are shaping the health and disease profiles in the world. Demographic ageing, rapid unplanned urbanization, and the globalization of unhealthy lifestyles such as tobacco use, unhealthy diet, inadequate physical activity and harmful alcohol use are universal trends, but the consequences are not evenly felt.

Developing countries have the greatest vulnerability and the least resilience. They are hit the hardest and have the least capacity to cope. These trends have tremendous implications at a time when the international community is pursuing better health as a poverty-reduction strategy. The costs of treatment and care for CVD events such as heart attacks and strokes can be catastrophic for patients, driving many millions of households below the poverty line each year. The growing CVD epidemic is also an impediment to economic development due to its impact on labour productivity and health care costs.

At present, many countries focus primarily on the care of acute cardiovascular events or complications of CVD. Sophisticated and costly technologies are often used for this purpose ignoring prevention and simple inexpensive interventions which can be implemented in primary care. This short-sighted approach will result in upward spiralling health care budgets, due to increasing number of people who develop CVD. The only solution lies in an integrated public health approach. Such an approach has to focus on behavioural risk factors and determinants that lie outside the health sector. People have to be provided opportunities for healthy eating and physical activity and deterrents for tobacco use through upstream policy actions. These measures need to be complimented with equitable health services for prevention, through a total risk approach and acute and long-term care for cardiovascular disease.

Today, we have a global noncommunicable disease strategy and an action plan, endorsed by 193 Member States. It provides a roadmap for our work, the work of our Member States and our partners under six main objectives.

1. The World Health Organization (WHO) is joining efforts with all partners to get NCD /CVD on the global health and development agenda so that NCD will be the subject of a resolution at the UN General Assembly in September 2010.

2. WHO is promoting coordinated national health strategies and action plans against major NCDs including CVD with a special focus on low and middle income countries. Under an overarching NCD prevention and control policy, national programs with performance targets need to be established in all countries for monitoring of risk factors, early detection and management of cardiovascular risk including diabetes and prevention of recurrences of cardiovascular disease.

3. Prevention of major cardiovascular risk factors is a WHO priority reflected in the global public health: instruments such as the Framework Convention on Tobacco Control (FCTC), Diet and Physical Activity Strategy and the proposed global strategy against the harmful use of alcohol which will discussed at the World Health Assembly in 2010.

4. There is a clear need for bridging gaps in knowledge about what works in NCD prevention and control. A prioritized NCD/CVD research agenda which addresses the priority needs of CVD prevention and control will be finalized in 2010. The aim is to provide guidance to developing countries on implementation research for effective translation of already available scientific evidence to action.

5. The recently established global NCD network (NCDnet) has facilitated partnerships processes across diseases linking CVD advocates with their colleagues from cancer, diabetes and lung diseases to jointly be more effective and to promote innovative resource mobilization mechanisms.

6. We need to know more precisely the extent of the NCD/CVD burden, its trends and determinants through reliable monitoring and evaluation programs at country level.

The mandate of the World Health Organization is to strengthen the capacity of all countries to realize the full potential of prevention and curtail unnecessary human suffering caused by disease through equitable and sustainable policies and programs.

Vascular Cognitive Impairment

John O'Brien

Dementia is a huge and growing public health burden, affecting 25 million people worldwide and with prevalence set to triple over the next 50 years with increasing longevity. Although Alzheimer's disease (AD) is responsible for around 60% of cases, vascular dementia (VaD) is the second commonest cause accounting for around 20% cases. The traditional view of

two entirely different disorders, with different aetiologies and outcomes, is now recognised as too simplistic for a number of reasons. Cerebrovascular disease is also recognised as an additional pathology with major clinical impact in those whose dementia is primarily due to AD, and vice versa, while vascular factors are also important aetiological factors for AD pathology. However, progress in the field has been limited by difficulties in terminology, for example use of the term dementia necessitates the presence of memory impairment, which is the norm in AD but not in cognitive disorders associated with cerebrovascular disease. The term vascular cognitive impairment (VCI) has been proposed to recognise the broad spectrum of cognitive, and indeed behavioural, changes associated with vascular pathology. It is characterised by a specific cognitive profile, with predominantly attentional and executive impairments, together with particular non-cognitive features (especially depression) and a relatively stable course, at least in clinical trial populations. Subtypes of VCI have been proposed, based on clinical and pathological differences, including cortical, subcortical, strategic infarct, hypoperfusion, haemorrhagic and mixed (with AD) type. Diagnostic criteria are emerging but require refinement and validation, especially for mixed dementias. There remain fundamental gaps in our understanding of pathophysiology, predicting prognosis and outcome and in therapeutics. Clinical trials to date, mainly in populations selected using currently accepted criteria for vascular dementia, have unfortunately generally been disappointing. A relatively modest cognitive benefit of agents such as nimodipine, memantine and cholinesterase inhibitors has been reported, though the clinical significance of these improvements remains to be established. Risk factor modification may be a useful strategy, and there is emerging evidence that hypertension is associated with increased rates of brain atrophy and cognitive decline while white matter lesions are an important predictor of subsequent functional decline. Further studies, focusing on particular subtypes of VCI and involving subjects at earlier stages of the disease, are required.

The Importance of Diet, Obesity and Type II Diabetes for Vascular Disease

Arne Astrup

Obesity, the metabolic syndrome, pre-diabetes and type 2 diabetes are important risk factors for the development of coronary artery disease and stroke (cardiovascular disease, CVD). Obesity, physical inactivity, diet composition, short sleep duration, and smoking are the most important risk factors for type 2 diabetes, and moderate alcohol and coffee consumption exerts a weak protective effect. Excessive body weight together with inactivity can account for almost 90% of all new cases of type 2 diabetes. So prevention and treatment of weight gain, excessive body weight and the metabolic syndrome are the cornerstones of prevention of type 2 diabetes. The major risk factors for weight gain and obesity are sedentary lifestyle with little physical activity, impaired or short sleep duration, and an inappropriate diet. The dietary risk factors are large portion sizes, sugar-rich soft drinks, high intakes of energy-dense foods poor in fibre and whole grain, including low intakes of fruit and vegetables. The optimal diet for prevention of weight gain provides 20-25% of energy from protein (low-fat meat, dairy, fish, shelfish, game, protein from plants; peas, beans etc.), 25-30% of energy from fat (high ratio of polyunsaturated to saturated), and 45-55% from fibre-rich, whole-grain carbohydrates characterised by a low glycemic index. Moderate amounts of alcohol from beer and wine contribute to the prevention of type 2 diabetes and CVD, but should be recognised and a contribution to total energy intake. The dietary advises for obesity and type 2 diabetes are fortunately the same that are considered to be the optimal for prevention of CVD.

Pierre Amarenco is Chairman of the Department of Neurology and Stroke Centre at the Bichat Hospital, and Professor of Neurology at Xavier Bichat Medical School and Denis Diderot University in Paris, France. His principal research interests concern cerebrovascular diseases. He is especially interested in the management of acute ischaemic stroke, and in the prevention of secondary stroke. Dr. Amarenco has been an investigator in the Etude du Profil Genetique de l'Infarctus Cerebral (GENIC) Study, the Blockade of the Glycoprotein IIb/IIIa Receptor to Avoid Vascular Occlusion Trial, and the French Study of Aortic Plaques in Stroke (FAPS) Study. He is a member of the French Society of Neurovascular Disorders and the New England Medical Centre Posterior Circulation Registry. Dr. Amarenco was awarded several times during his career, with notably the Award of the Second European Stroke Conference (1992) and recently the Jean-Paul Binet award (Clinical Research in Cardiovascular Diseases) of the Medical Research Foundation (2001). He has actively taken part in redaction of more than 150 publication and articles on cerebrovascular disease in journals such as Circulation, the Journal of Neurology, Stroke, Chest, Neurology, Cerebrovascular Diseases, the American Heart Journal, and Blood.

Arne Vernon Astrup, M.D., Dr.Med.Sci., is Head of The Department of Human Nutrition at The Faculty of Life Sciences, University of Copenhagen, Denmark. He was awarded the Chair in Nutrition at the University in 1990. Arne Astrup is Director of the Danish Nordea Foundation OPUS research centre 2009-14. After receiving his medical degree from the University of Copenhagen in 1981 Arne Astrup completed residencies in internal medicine at the Glostrup and Hvidovre Hospitals in Copenhagen. He attained a Doctorate in Medical Science at The University of Copenhagen in 1986. Arne Astrup's main areas of interest and research include physiology and pathophysiology of energy and substrate metabolism, with a special emphasis on the etiology and treatment of obesity. The research of Arne Astrup and his group covers an extensive area. Major research collaboration includes participation in the EU multicenter studies: EUROSTARCH, CARMEN, NUGENOB, DIABESITY, DIOGENES, EMOB, and HEALTHGRAIN. Arne Astrup has written/co-authored over 330 original scientific papers and reviews published in international peer reviewed journals, including papers in *The Lancet*, *British Medical Journal*, and *The Journal of Clinical Investigation*. Citation H-index: 52. He has contributed to over 700 other scientific publications, such as textbook chapters, scientific abstracts and letters. He is President of The International Association for the Study of Obesity (IASO) 2006-09, and Editor-in-Chief of the IASO journal *Obesity Reviews*. He is a member of the editorial boards of *The International Journal of Obesity* and *The Journal of the Danish Medical Association*. Arne Astrup was made Knight of the Order of Dannebrog in 1999. Awards received include Servier's Award for Outstanding Obesity Research in 1990; IASO André Mayer Award 1994; Danone Chair in Nutritionat The University of Antwerp 2002; The Faculty of Life Sciences, University of Copenhagen Communication Prize 2007; International Association of Business Communicators 2009 EME Excel Merit Award for Communication Leadership.

Nicolò Boncompagni-Ludovisi, Prince of Piombino, Prince of the Holy Roman Empire, Prince of Venosa etc.; Knight of the Sovereign Order of Malta, and of the Constantinian Order, Chemical Engineer of the E.T.H. (Federal Polytechnicum in Zürich-Switzerland). Roman Catholic. Born in Rome (Italy) January 21,1941. Studied in Rome and then attended an international boarding school (German speaking) in Switzerland (Lyceum Alpinum in Zuoz, Engadin Switzerland). Studies all in German language. After the A Levels went to the ETH (Eidgenoessische Technische Hochschule) i.e. Polytechnicum in Zürich Switzerland where he attained in 1965 under Prof. dr. Vladimir Prelog (Nobel Prize for Chemistry) the Master's degree in Chemistry and the title of Chemical Engineer. 1990-1995 was appointed as an international consultant to the Russian Minister of Foreign Trade Relations. 1991-1995 established laboratories in Russia which produced computer software which was then sold in western Europe. Presently he develops his land properties near Rome and restores the historical 500 years old Villa Aurora in Rome which derives its name from Guercino's masterpiece; Villa Aurora was, in the 16th century, a country retreat where famous artists, musicians and scientists and literary geniuses gathered under the patronage of Cardinal Francesco Maria del Monte first and in the 17th century under the patronage of Cardinal Ludovico Ludovisi. Villa Aurora was in fact sold by Cardinal Francesco Maria del Monte to Cardinal Ludovico Ludovisi nephew of Pope Gregory XV in 1621. The Villa is now owned by the Prince of Piombino XIII, Nicolò Boncompagni Ludovisi. Languages: English, French, German, Italian, Spanish, Swiss German, basic Russian.

Eugene Braunwald, M.D. is the Distinguished Hersey Professor of Medicine at Harvard Medical School, and Chairman of the TIMI Study Group at the Brigham and Women's Hospital. Dr. Braunwald received his medical training at New York University and completed his Medical Residency at the Johns Hopkins Hospital. He served as the first Chief of the Cardiology Branch and as Clinical Director of the National Heart, Lung and Blood Institute, founding Chairman of the Department

of Medicine at the University of California, San Diego. From 1972 to 1996 he was Chairman of the Department of Medicine at the Brigham and Women's Hospital. He was a founding trustee and Chief Academic Officer of Partners HealthCare System. Dr. Braunwald's first major paper was published in Circulation Research in July 1954, and he has been a major force in cardiology in the past half century. His early work focused on the control of ventricular function and he was the first to measure both left ventricular ejection fraction and left ventricular dp/dt in patients. His group showed the first neurohumoral defect in human heart failure, defined the pathophysiology of hypertrophic cardiomyopathy and demonstrated salvage of ischemic myocardium following coronary occlusion. They defined myocardial stunning and ventricular modeling following myocardial infarction. For the past 24 years, as Chairman of the TIMI Study Group, he and his colleagues demonstrated improved patient survival with a patent coronary artery which led to the widely accepted "open artery hypotheses". They were the first to show the benefit of preventing adverse remodeling of the infarcted ventricle with ACE inhibition. In the PROVE-IT TIMI 2 Trial, in 2004, they demonstrated the benefit of more intensive reduction of LDL in high risk coronary artery patients, which has already changed practice guidelines and will favorably affect the lives of millions. Dr. Braunwald is and has been an editor of *Harrison's Principles of Internal Medicine* for 12 editions, and the founding editor of *Heart Disease*, now in its 8th Edition, the most influential textbooks in their fields. *Science Watch* listed Dr. Braunwald as the most frequently cited author in Cardiology; he has an H index of 175. Based on his contributions, Dr. Braunwald has received numerous honors and awards including the Distinguished Scientist Award of the American College of Cardiology, Research Achievement, and Herrick Awards of the American Heart Association, the Gold Medal of the European Society of Cardiology and is the recipient of fifteen honorary degrees from distinguished universities throughout the world. The living Nobel Prize winners in medicine voted Dr. Braunwald as "the person who has contributed the most to cardiology in recent years". Dr. Braunwald was the first cardiologist elected to the National Academy of Sciences of the United States.

Louis R. Caplan, M.D. was born in Baltimore, Maryland December 31, 1936. He attended Williams College in Williamstown, Massachusetts and graduated cum laude in 1958. Although he was a pre-med student he majored in history and was the recipient of the Williams College history prize. He attended the University of Maryland Medical School in Baltimore and graduated in 1962 summa cum laude. He was an intern and junior resident in Medicine at the Boston City Hospital from 1962 to 1964. During that time, he decided to become a Neurologist. After his internship and junior residency in Medicine, he served 2 years in the US Army as an internist but worked in the neurology clinic. He then returned to Boston and did his Neurology residency from 1966 to 1969 on the Harvard Neurological Unit at the Boston City Hospital under Dr. Denny-Brown. His background in internal medicine and Neurology and the complexities of cerebrovascular disease led him to decide that stroke was to be his major life's work. During the 1969-1970 year he was a Cerebrovascular Disease Fellow at the Massachusetts General Hospital with Dr. C. Miller Fisher, who at that time was the outstanding stroke clinician in the USA. In July 1970, he became a staff Neurologist at the Beth Israel Hospital in Boston and Assistant Professor of Neurology at Harvard Medical School. He devised the first registry in cooperation with Dr. Jay P. Mohr at the Massachusetts General Hospital. With Dr. Mohr he founded and reported the results of the Harvard Cooperative Stroke Registry in 1978. That same year he moved to Chicago to become Neurologist-in-chief at the Michael Reese Hospital and Professor of Neurology at the University of Chicago. There he continued his work on stroke and became interested in racial differences in stroke subtypes and vascular lesions. He returned to Boston in 1984 to become Neurologist-in-chief at the New England Medical Center and Professor and Chairman of the Department of Neurology and Professor of Medicine at Tufts. He remained at Tufts until January 1998, when he returned to the Beth Israel Hospital and Harvard Medical School. He is currently Professor of Neurology at Harvard Medical School and Chief of the Stroke Service at the Beth Israel Deaconess Medical Center.

Geoffrey Donnan, MB BS, MD, FRACP, FRCP(Edin) is Professor of Neurology, University of Melbourne, Director of Neurology Austin Health, and Director of the National Stroke Research Institute in Australia. He is an Honorary Principal Fellow of the Howard Florey Institute. He co-founded the Australian Stroke Trials Network (ASTN) which has numerous investigator driven and commercially sponsored stroke trials. Subsequently he also co-founded Neuroscience Trials Australia to enhance Australian commercial and investigator-driven clinical trial capability. He is Past President of the Stroke Society of Australasia and Past President of the Australian Association of Neurologists. He has over 300 peer reviewed journal publications, 51 book chapters, edited 15 proceedings of national meetings, edited/authored three books, and sits on editorial boards of seven international journals including Lancet Neurology, Section Editor for Stroke and Associate Editor of Cerebrovascular Diseases. Dr. Donnan's research interests include neuroimaging and clinical stroke trials including acute studies and secondary prevention.

Conrado J. Estol was born in 1959 in New York City, NY (USA). He obtained an MD and a PhD (summa cum laude) from the School of Medicine at the Uni-

versity of Buenos Aires, Argentina. Dr. Estol was trained in Internal Medicine at Mount Sinai Hospital (NY), completed a Neurology Residency at Presbyterian University Hospital (Pittsburgh University, Pennsylvania) and was a Stroke Fellow at the New England Medical Center Hospital and Spaulding Rehabilitation Hospital (Tufts University and Massachusetts General Hospital in Boston). He is certified by the American Board of Psychiatry and Neurology. Dr. Estol is presently Director and Founder of the Neurological Center for Treatment and Research. His main areas of clinical and research interest include cerebrovascular disease, neurological intensive care, cognitive dysfunction and headache. Dr. Estol is Associate Editor of the International Journal of Stroke and has participated in the Editorial Board of several international journals. He is founder and President of the Argentine Cerebrovascular Association and was President of the Harvard Club Argentina. Among other memberships, Dr. Estol is Fellow of the American Academy of Neurology (AAN), a member of the American Neurological Association and has received several awards including the International Affairs Committee Award of the AAN and the Young Investigator's Award of the International Stroke Society. Dr. Estol has over 150 Journal and Book Chapter publications and has given over 130 international invited lectures.

Valentin Fuster serves The Mount Sinai Medical Center as Director of Mount Sinai Heart, the Zena and Michael A. Wiener Cardiovascular Institute and the Marie-Josée and Henry R. Kravis Center for Cardiovascular Health. He is the Richard Gorlin, MD/Heart Research Foundation Professor, Mount Sinai School of Medicine. Dr. Fuster was the President of Science and is now the General Director of the Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC) in Madrid, Spain. Among the seemingly countless positions of distinction that he holds are Past President of the American Heart Association, Past President of the World Heart Federation, Member of the Institute of Medicine of the National Academy of Sciences where he serves as Chair of the committee on Preventing the Global Epidemic of Cardiovascular Disease, former member of the National Heart, Lung and Blood Institute Advisory Council, and former Chairman of the Fellowship Training Directors Program of the American College of Cardiology. Twenty-six distinguished universities throughout the world have granted him Honorary Doctorate Degrees. Dr. Fuster is the recipient of two major ongoing NIH grant. He has published more than 790 Pubmed articles on the subjects of coronary artery disease, atherosclerosis and thrombosis, and he has become the lead Editor of two major textbooks on cardiology, 'The Heart' (previously edited by Dr. J. Willis Hurst) and 'Atherothrombosis and Coronary Artery Disease' (with Dr. Eric Topol and Dr. Elizabeth Nabel). Dr. Fuster has been appointed Editor-in-Chief of the Nature journal that focuses on cardiovascular medicine (Nature Reviews, Cardiology, April 2009) and he is the Editor of the new 'AHA Guidelines and Scientific Statements Handbook', which compiles all the latest information. Dr. Fuster is the only cardiologist to receive the two highest gold medal awards and all four major research awards from the four major cardiovascular organizations: The Distinguished Researcher Award (Interamerican Society of Cardiology, 2005 and 2009), Andreas Gruntzig Scientific Award and Gold Medal Award (European Society of Cardiology, 1992 and 2007 respectively), Gold Medal Award and Distinguished Scientist (American Heart Association, 2001 and 2003 respectively), and the Distinguished Scientist Award (American College of Cardiology, 1993).

Werner Hacke, MD, PhD Dsc (hon) FAHA FESO, is Professor and Chairman of the Department of Neurology at the University of Heidelberg in Germany. He received his Neurology training at the University of Aachen, Germany and at the University of Bern, Switzerland. After one year as visiting scientist at the Scripps Research Foundation in La Jolla, California, he took the Chair of Neurology at Heidelberg in 1987. He was Dean of Medicine of the University of Heidelberg, Germany, between 1990 and 1993 and 1995-1996. His main scientific and clinical interest is in stroke and critical care neurology. He has pioneered the field of thrombolysis for acute stroke and initiated several new management options for large infarctions including hypothermia and decompressive surgery. He was the President of the German Neurological Society (2001-2002), the President of the German Interdisciplinary Society of Critical Care Medicine (2003-2004) and the German Stroke Society (2008-2009). He is the founding President of the European Stroke Organisation (ESO), 2008. He is now the First Vice President of the World Federation of Neurology. In 1998 he was the first European recipient of the Feinberg award for Excellence in Stroke Research, given by the American Stroke Association and the first recipient of the Karolinska Stroke Award in 2004. He was awarded the Pette Medal, the highest award of the German Neurological Society in 2008. He received the Presidents Award by the World Stroke Organisation (2008), the Mihara Award by the Mihara Foundation (Japan, 2009), and the Jarecki Award (USA, 2009). Prof Hacke is honorary member of several national societies of Neurology, including the American Neurological Association (ANA), the Pan Russian Society of Neurology and the French Neurological Society, and holds an honorary doctorate in Tblisi, Georgia. Prof. Hacke has published 300 original articles listed in pubmed and SCI.

Daniela Jezova, Vice-president of the Slovak Academy of Sciences, Senior Researcher of the Institute of Experimental Endocrinology, Professor of Pharmacology at the Medical School, Comenius University, Bratislava, Slovakia. Publications: more than 200, mostly in

peer review international journals. Citations: more than 2000 SCI/WOS, Hirsch index 29. Invited meeting presentations: more than 70. Field of research: She is internationally recognized for her work in stress research including investigation of risk factors for cardiovascular and brain diseases, in the fields of neuroendocrinology, physiology and psychopharmacology particularly in relation to stress hormones and psychiatric disorders both in clinical studies and animal models. Scientific Grants: Coordination of a successful EU Centre of Excellence project in 5FP. Scientific School: supervisor of 12 completed and 2 running PhD theses in pharmacology or physiology; Scientific Boards: serving as expert for projects of the 6th an 7th FP for EC; referee for high impact international journals; assistant editor in journal Neuroendocrinology. Membership in Scientific Societies: President of the Slovak Physiological Society, Scientific Secretary of the Czech Neuropsycho-pharmacological Society, member of the Central Eastern European Committee of the Collegium Internationale of Neuropsychopharmacology, member of the Academia Europaea. Honours and Awards: Prestigious national prize Crystal Wing for Medicine and Science, Gold Medal of the Slovak Medical Society, Gold Medal of the Faculty of Medicine of the Comenius University, Gold Jessenius Medal for advances in medical sciences, Charvat's Lecture, Slovak Endocrinological Society, Purkyn's Lecture, Slovak Physiological Society. Familiar status: Married, two children.

Walter J. Koroshetz, M.D. was named Deputy Director of NINDS in January of 2007. He works with the NINDS Director in program planning and budgeting, and oversees Institute scientific and administrative functions. Before joining NINDS, Dr. Koroshetz served as vice chair of the neurology service and director of stroke and neurointensive care services at Massachusetts General Hospital (MGH). He was also a professor of neurology at Harvard Medical School and has led neurology resident training at MGH since 1990. A native of Brooklyn, New York, Dr. Koroshetz graduated from Georgetown University and received his medical degree from the University of Chicago. He trained in internal medicine at the University of Chicago and Massachusetts General Hospital. Dr. Koroshetz trained in neurology at MGH, after which he did post-doctoral studies in cellular neurophysiology at MGH and the Harvard neurobiology department. He joined the neurology staff, first in the Huntington's Disease unit and then in the stroke and neurointensive care service. As a member of the NINDS intramural review and oversight committees, Dr. Koroshetz has been involved in various NINDS symposia and clinical trials, and served as the Institute's representative to the American Neurological Association's Career Development Symposium. He was a member of the NINDS-chaired Brain Attack Coalition (BAC), a group of professional, voluntary and governmental entities dedicated to reducing the occurrence, disabilities, and death associated with stroke.

Attilio Maseri (Udine, 1935) obtained his degree in Medicine and Surgery from Padua University in 1960 and specialised in Cardiology and Nuclear Medicine at Pisa University. He continued his studies in the USA at Columbia University in NYC, working with Nobel laureate Dr. A. Cournald. In 1967 he became associate professor of special medical pathology and Head of the Coronary Research Centre of the Italian National Research Council in Pisa. In 1979 he became full professor of Cardiovascular Medicine at the Royal Postgraduate Medical School in London and Director of Hammersmith Hospital. In 1991 he returned to Rome and became full professor at the Catholic University and Director of the Cardiology Institute of the 'Gemelli' Polyclinic. From 2001-2008 he was full professor of cardiology at Vita-Salute San Raffaele University and Director of the Cardio-Thoracic-Vascular Department at San Raffaele Hospital in Milan. From 2004-2007 he was the President of the Italian Federation of Cardiology. Since January 2008 he has been the President of Heart Care Foundation, the Italian Foundation for the Fight against Cardiovascular Diseases of the National Association of Hospital Cardiologists). He is a member of the Johns Hopkins Society of Scholars (1998). During the course of his career he was also the cardiologist of Queen Elizabeth II of England and Pope John Paul II. He is the single author of a textbook on cardiology entitled 'Ischemic Heart Disease – Rational Basis for Clinical Practice and Clinical Research' (Churchill – Livingstone New York 1995). He has also published over 750 articles in international journals and has received numerous prizes and honours, including the King Faizal International Prize in Medicine (1992), the 'Distinguished Scientist Award' of the American College of Cardiology (1997), the Premio Invernizzi for Medicine (1998), the Grand Prix Scientifique de l'Institut de France (2004), the Medal of the Italian President of the Republic. Pope John Paul II appointed him Commendatore of the Order of St Gregory the Great and in 2005 he became a Knight of the Grand Cross of the Order of Merit of the Republic of Italy. He was among the first five Europeans called to the Editorials Board of the New England Journal of Medicine. He currently coordinates a series of clinical research projects on the biological causes that trigger the acute coronary instability that leads to heart attacks, and on the biological mechanisms of myocardial damage and ways to repair it.

Shanthi Mendis, MBBS, MD, FRCP, FRCPE, FACC, commenced her medical career in Bristol, England in 1974 and worked in the UK in the NHS for 6 years. She had her post doctoral training in Scotland and USA for 4 years. Subsequently she worked in Sri Lanka and, prior to being recruited to WHO in 1998, was the Professor and Head, Department of Medicine, Faculty of Medicine, University of Sri Lanka. As Senior Adviser in Cardiovascular Diseases at the World Health Organization HQ, Geneva Switzerland, she has gained extensive experience in pro-

viding technical support to developing countries for policy and programme development. At present she also coordinates the global programs on prevention and management of Noncommunicable diseases. She is a Fellow of the Royal College of Physicians of Lond. and Edin. and Fellow of the American College of Cardiology. She has extensive public health, teaching, clinical and research experience and has published widely.

John O'Brien's research interests include: the application of MR, SPECT and PET imaging in dementia and depression; neurobiological changes (in particular the role of vascular factors) in late-life affective disorders and cognitive impairment; dementia with Lewy bodies; clinical trials. His group is undertaking serial imaging (structural and functional MR, blood flow and ligand SPECT and PET) studies on subjects with Alzheimer's disease (AD), dementia with Lewy bodies, Parkinson's disease (PD) and PD dementia to elucidate i) relationships and imaging correlates of diagnosis and symptoms ii) usefulness in improving accuracy of differential diagnosis iii) markers of early diagnosis and iv) how structural and chemical changes alter with disease progression. His current research projects include a MRC-funded study of cognitive dysfunction after stroke, a study of MR imaging in AD and DLB funded by the Jules Thorne Foundation, a study of functional MRI funded by the Alzheimer's Research Trust, an Alzheimer's Research Trust Fellowship to Dr Emma Burton (investigating the neuropathological basis of MR changes), a study of autonomic and imaging changes in late life depression, and a study of predictors of dementia in Parkinson's disease. Prof. O'Brien is also the Clinical Lead for North East Dementia and Neurodegenerative Diseases Clinical Research Network, Deputy Editor International Psychogeriatrics, Board Member of the International Psychogeriatric Association, Head of Northern Deanery Postgraduate School of Psychiatry, Lead Consultant for Newcastle Memory Clinic, President of the International College for Geriatric Psychoneuropharmacology (ICGP) and Member of Vas-Cog Executive Committee.

Cristiana Paoletti del Melle, MD has graduated in the University of Rome with highest honors and laude. Specialized with highest honors and laude in Cardiology, Endocrinology, Gastroenterology, Neuropsychiatry, Psychiatry Forensic and Criminology, Legal Medicine. Expert in Gender Medicine. Coordinator of the Medical and Emergency staff of the Italian Parliament for 20 years. Currently she is Coordinator of the Medical College of the Senate of the Republic. Member of Scientific Committee of Italian NIH. Consultant of the Minister of Health for Multimedial Communication.

Terje R. Pedersen, MD is a certified specialist of internal medicine and cardiology, Professor of Medicine (Preventive Cardiology) at the University of Oslo, Norway and Head of the Centre for Preventive Medicine at Oslo University Hospital, Ullevål. His main interest is in preventive cardiology and he has been the principal investigtor in several major clinical trials like The Norwegian Timolol Trial, the Scandinavian Simvastatin Survival Study (4S), the IDEAL study to determine whether lowering of cholesterol beyond what was achieved in the 4S is beneficial for CHD patients and the SEAS study to investigate the effect of cholesterol lowering in patients with aortic valve stenosis . He is currently involved in several intrnational collaborative clinical trials in the field of preventive medicine as a member of Executive Committees, Steering Committees and Data Safety and Monitoring Committees.

Patrizio Polisca (born 11 December 1953 in the Italian region of Marche) is a specialist in cardiology, anaesthetics and reanimation and a professor at the Cardiosurgery Institute of Tor Vergata University in Rome. In June 2009 he was appointed vice director of the Department of Health and Welfare of the Governatorate of the Vatican City State and is the Pope's personal physician. He is also the President of the Medical Consultation Unit of the Congregation for the Causes of Saints.

Giovanni M. Rocchi was born in 1939 in Rome, Italy, and is married with a son and a daughter. He obtained his MD from 'La Sapienza' University of Rome in 1963 and his PhD from the same University. He graduated from the Departments of Infectious Diseases and Internal Medicine in Rome, and was promoted to Associate Professor in 1983. In 1985, he became Professor and Chairman of the Department of Infectious Diseases. He is currently Professor of Medicine at 'Tor Vergata' University Medical School in Rome where he holds the Chair of Infectious Diseases in Internal Medicine. Since 1967, Prof. Rocchi has been consultant physician in internal medicine in the clinical department of the Vatican City. Since July 2005, he has been in charge of the Direzione di Sanità ed Igiene of the Vatican City where he acts as director with specific interest in the management of the clinical department. Prof. Rocchi's research and clinical interests are medical care in internal medicine and infectious diseases. He has authored over 150 publications and made contributions to several textbooks. He is a member of several professional societies, including the Italian Society of Internal Medicine and the Italian Society of Infectious and Tropical Diseases.

Allan H. Ropper is Professor of Neurology of Harvard Medical School and Executive Vice Chairman of the Department of Neurology at Brigham and Women's Hospital, Boston, Massachusetts. He was born in 1950 in New York, New York. He received his B.A. from Cornell University in Ithaca, New York and his M.D. from Cornell University Medical College in New York in

1974. Dr. Ropper trained in internal medicine at UCSF-Moffit Hospital and in neurology at Massachusetts General Hospital. His work has been mainly in the field of neurological intensive care and related disorders such as Guillain-Barrè Syndrome. His present focus includes studies of gene therapy as a potential treatment for peripheral neuropathy and he is conducting an NIH sponsored study of vascular endothelial growth factor (VEGF) for the treatment of diabetic neuropathy. He has over 150 publications and is an author of the most widely consulted textbook of neurology, Principles of Neurology, which is in its ninth edition. He is a longtime contributor to several major textbooks of medicine including 'Harrison's Principles of Internal Medicine'. He has received numerous awards for teaching and service. Dr. Ropper is an associate editor of the New England Journal of Medicine.

Felix Unger is an Austrian, born in March 1946. He is a Cardiac Surgeon at Paracelsus Medical University Salzburg. He attended the Medical Faculty of the University of Vienna and graduated 1971. After his graduation he trained at the University Clinic for Cardiology and the Clinic for Surgery at the University of Vienna to become a cardiac surgeon. In 1974 he visited the Texas Heart Institute, the Cleveland Clinic and the University of Salt Lake City where he invented a new type of artificial heart. In 1978 he became Univ. Dozent at the University of Vienna. In 1979 he moved to Innsbruck University, where he established the Coronary Artery Surgery programme. In 1983 he became Professor of Cardiac Surgery. In 1985 he moved to Salzburg, where he established a new centre for Cardiac Surgery at the Paracelsus University for Medicine, the University Clinic for Cardiac Surgery. Out of his enormous experience in cardiac surgery his specific scientific interest has been in replacing the heart in all forms and assist devices. In 1986 he implanted in Salzburg the First Artificial Heart with a consecutive Heart Transplantation. Beside these efforts in Assisted Circulation he focused on clinical topics, as the gastro-epiploic artery as new device. He also worked in the area of artificial blood. His main specific interest is Coronary Artery Surgery. When in the 1990s stenting became a new alternative to Surgery, he directed the surgical arm in the ARTS-study, a randomized study enrolling 1.200 patients. In 1997 he founded the European Heart Institute for monitoring cardiac interventions in Europe. Overall he has written/co-authored over 450 publications in the most important journals in the field such as the New England Journal of Medicine, Cardio and Thoracic Surgery, Circulation, European Heart Journal, and he has edited 17 books on Surgery. He is a member of all mayor national and international societies in his field, member of 8 different Academies of Sciences and his work has been awarded 8 Honorary Doctor Degrees. In 1990 he founded with Cardinal König and Nikolaus Lobkowicz the European Academy of Sciences and Arts, the Academia Scientiarum et Artium Europaea. Since 1990 he has been the president of the Academy which has 1.400 members mainly in Europe. Its mission is to contribute to the future of Europe and its unity by promoting knowledge, cooperation and tolerance. Prof. Unger is married to Monika von Fioreschy, father of two sons and grandfather to one grandchild.

For the biographies of the other Academicians of the PAS, cf. Pontificia Academia Scientiarvm, *Yearbook* (Vatican City 2008), p. 15 ff.

LIST OF PARTICIPANTS

Prof. Pierre Amarenco
Professor of Neurology at Xavier Bichat
Medical School and Denis Diderot University
Paris (France)

Prof. Arne V. Astrup
Director
Department of Human Nutrition
University of Copenhagen
(Denmark)

Prof. Eugene Braunwald, MD
Distinguished Hersey Professor of Medicine
Harvard Medical School
Chairman, TIMI Study Group
Brigham and Women's Hospital (USA)

H.S.H. Prince Nicolò Boncompagni-Ludovisi
Chemical Engineer
Property Developer
(Italy)

Prof. Nicola Cabibbo
President
The Pontifical Academy of Sciences
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University of Melbourne
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Dr. Conrado J. Estol, MD, PhD, FAAN
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Neurological Center for Treatment
and Research, Buenos Aires
(Argentina)

Prof. Valentín Fuster, MD, PhD
Director
Mount Sinai Heart
Mount Sinai Medical Center
(USA)

Prof. Werner Hacke, MD, PhD
Chairman
Department of Neurology
University of Heidelberg
(Germany)

Prof. Daniela Ježová, PharmD., DSc.
Head of Laboratory and Scientific Secretary,
Institute of Experimental Endocrinology
Bratislava (Slovak Republic)

Dr. Walter J. Koroshetz
Deputy Director
National Institute of Neurological Disorders
and Stroke (NINDS)
Bethesda, MD (USA)

Prof. Attilio Maseri
President
Heart Care Foundation ONLUS
Milan (Italy)

Dr. Shanti Mendis, MD
Senior Adviser Cardiovascular Diseases
Coordinator, Chronic Disease Prevention and
Management; World Health Organization,
Geneva (Switzerland)

Prof. John O'Brien
Professor of Old Age Psychiatry
Institute for Ageing and Health
Newcastle University (UK)

Dr. Cristiana Paoletti del Melle, MD
Gender Medicine, Coordinator Medical
College of Republic Senate;
Member of Scientific Commitee of Italian
NIH; Scientific Journalist, Rome (Italy)

Prof. Terje R. Pedersen, MD, PhD
Professor of Medicine (Preventive
Cardiology), University of Oslo
(Norway)

Prof. Patrizio Polisca
Vice Director
Department of Health and Welfare
(Vatican City)

Prof. Giovanni M. Rocchi
Director
Department of Health and Welfare
(Vatican City)

Dr. Allan H. Ropper, MD, FRCP, FACP, FAAN
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The Brigham and Women's Hospital (BWH)
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H.E. Msgr. Prof. Marcelo Sánchez Sorondo
Chancellor
The Pontifical Academy of Sciences
(Vatican City)

Univ.Prof.Dr.Dr.h.c. Felix Unger
Paracelsus Medical University Salzburg
President, European Academy
of Sciences and Arts
(Austria)

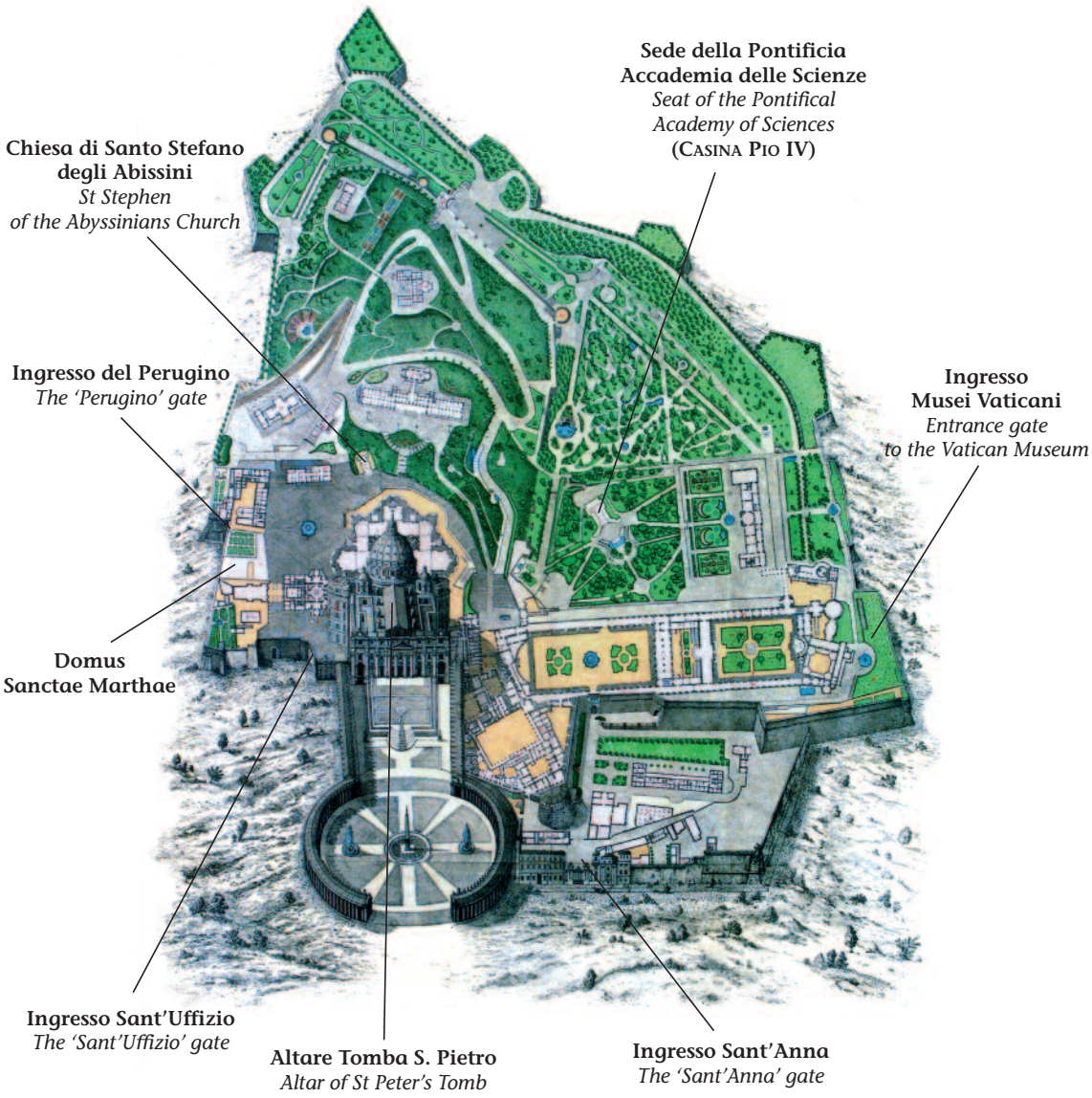
Memorandum

– Every day a bus will leave the Domus Sanctae Marthae for the Academy, fifteen minutes before the beginning of the session. A bus will depart from the Academy after dinner at the end of the afternoon sessions to take participants back to the Domus Sanctae Marthae. Lunch and dinner for the participants will be served at the Academy every day except dinner on Tuesday.

– On Tuesday, a bus will take the participants from the Casina Pio IV at the end of the Round Tables to the concert and dinner at the residence of Prince Boncompagni and back.

– On Wednesday, for those wishing to attend, there will be the General Audience with the Holy Father Benedict XVI at 9:30 in Saint Peter's Square.

Note
Please give your **form for the refunding of expenses** to the secretariat at least one day before your departure so that you can be refunded immediately.



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by Lorenzo Rumori