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This supplement
includes the summary of
symposium 1, presented
during the 14th MLAVS
Congress in Portoroz



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NEWS IN ANGIOLOGY AND VASCULAR SURGERY IN THE MEDITERRANEAN REGION

**This supplement includes the summary of
symposium 1, presented during the 14th MLAVS
Congress in Portoroz**

WHAT IS NEW IN ANGIOLOGY

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ATHEROSCLEROSIS AND INFLAMMATION – becoming inseparable

There is more and more evidence suggesting that atherosclerosis should be considered an inflammatory disease (1). Inflammation seems to have a central role in initiation of atherogenesis as well as in destabilization of advanced atherosclerotic plaque that culminates in plaque rupture. Several risk factors, i.e., hemodynamic forces, hyperlipidemia, smoking, and others trigger the initial step of endothelial damage, which elicits an inflammatory response. Activated endothelial cells express vascular adhesion molecule-1 (VCAM-1) and P- and E-selectins. These molecules attract leukocytes/monocytes to a subendothelial tissue - a process governed by hemoattractant cytokines and chemokines. VCAM-1 expression is at least in part initiated by modified lipoprotein particles accumulating in the intima. This represents a direct link between hyperlipidemia and initiation of inflammation leading to progression of atherosclerosis. Proinflammatory cytokines are also produced by activated T-lymphocytes accumulating in the atheroma. Monocytes convert to macrophages in the intima, express several scavenger receptors and become foam cells. Activated macrophages increasingly express metalloproteinases that weaken the fibrous cap and thus predispose to plaque rupture. Several novel risk factors may be involved in triggering arterial wall inflammation, such as homocystein, Chlamydia pneumoniae, viruses, and certain adipokines. In addition, low levels of anti-inflammatory molecules, such as HDL, indirectly promote inflammation and atherogenesis. Involvement of inflammation in atherogenesis has been confirmed in different clinical studies. Individuals at high risk of atherosclerosis are reported to have high levels of inflammatory markers, such as interleukin-6, TNF- α and high-sensitive C-reactive protein (CRP). Among those, CRP has been proposed as an independent factor for cardiovascular disease and atherothrombotic events (2). Further, circulating markers of inflammation are related to worse prognosis of subjects with established atherosclerotic disease and are related to progression of peripheral arterial disease (PAD) (3, 4). In the study of Widnam and coworkers it has been found that in adult U. S. population inflammatory markers are strongly associated with PAD, independently of traditional risk factors (5). Similarly, in subgroup analysis of the Atherosclerosis Risk in Communities study it has been indicated that elevated inflammatory markers are associated with decreased ankle-brachial index (6).

Recognition of inflammation as a basic pathogenetic mechanism of atherosclerosis will probably influence treatment of this ubiquitous disease in the future. Treatment of atherosclerosis with antibiotics, based on the presumption that inflammation in the arterial wall can be caused by infection, did not give expected results. However, the anti-inflammatory activity of established antiatherogenic agents, like statins, may represent new therapeutic potential and may further clarify their beneficial effects in clinical trials. Other potential agents are new antiinflammatory drugs and angiotensin II inhibitors (7).

References

1. Ross R. Atherosclerosis – an inflammatory disease. *N Engl J Med* 1999; 115-26.
2. Napoli MD, Papa F, Bocola V. Prognostic influence of increased C-reactive protein and fibrinogen levels in ischemic stroke. *Stroke* 2001; 32: 133-8.
3. Poredoš P, Žižek B. Plasma viscosity increase with progression of peripheral arterial atherosclerotic disease. *Angiology* 1996; 47 (3): 253-9.
4. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Plasma concentration of C-reactive protein and risk of developing peripheral vascular disease. *Circulation* 1998; 97: 425-8.
5. Widman RP, Muntner P, Chen J, He J. Inflammatory markers and peripheral vascular disease in NHANES 1999-2000. *Circulation* 2004; 110: 810.
6. Reich LM, Boland LL, Hirsch AT. Elevated hemostasis and inflammatory markers are associated with decreased ankle-brachial index. *Circulation* 2004; 110: 810.
7. Čerček B. Atherosclerosis and inflammation – therapeutic application. Abstract book. 14th Congress of the Mediterranean League of Angiology and Vascular Surgery 2004: 15.

THERAPEUTIC ANGIOGENESIS – promise not yet fulfilled

For more than 8 years, therapeutic angiogenesis has been an eagerly awaited treatment for patients with critical limb ischemia who are not candidates for percutaneous or surgical revascularization – ever since Isner and co-workers published in 1996 their report on a 71-year old female patient with an ischemic right leg who developed new collateral vessels, spider angiomas and limb edema after intraarterial gene transfer of plasmid DNA encoding for vascular endothelial growth factor (VEGF) (1). Small, open-label, phase 1 trials have demonstrated the feasibility and safety of such an approach in patients with PAD, but those studies were not suited for efficacy assessment since they used no placebo-control subjects (2, 3). Results of the first phase 2, double-blind, placebo-controlled studies have not been overwhelmingly successful. In the TRAFFIC study, intrarterial fibroblast growth factor (FGF) increased peak walking time in claudicants by about 1 min in comparison to placebo at 90 days after infusion, and there was no difference between a single infusion or a repeated infusion of FGF at 30 days. The results were significant in an intention-to-treat analysis and in a pairwise comparison between placebo and single-dose, but not by ANOVA (4). The RAVE trial tested the efficacy of intramuscular application of adenoviral VEGF gene into lower limbs of claudicants. The peak treadmill walking time did not differ between the placebo, low-dose and high-dose group, and neither did the claudication onset time or quality-of-life measures (5). The results of VEGF and FGF protein or gene therapy have not been spectacular in improving myocardial perfusion, either. Recently, AGENT 3 investigators have reported that intracoronary infusion of adenoviral FGF-4 gene in patients with stable angina did not improve exercise time in comparison to placebo, although there has been a positive trend toward improvement with the high dose in older patients, those with worse angina and in females (6). What is the reason for the – at least relative – failure of therapeutic angiogenesis at its present stage? It has been suggested that for successful tissue revascularization an “angiogenic switch” has to be turned on, i.e., a transition from angiogenesis (disorderly proliferation of endothelial cells, forming fragile and leaky microvessels) into

arteriogenesis (including orderly recruitment of smooth muscle cells, forming mature, stable and functional vessels) is necessary. Placental growth factor and its receptor, vascular endothelial growth factor receptor-1, have become novel targets for research in this area (7). Pro-arteriogenic effects have been ascribed also to granulocyte/macrophage colony stimulating factor (GM-CSF) that is under investigation in claudicants in a randomized, double-blind study – the START trial – in the Netherlands (8).

References

1. Isner JM, Pieczek A, Schainfeld R, Blair R, Haley L, Asgara T, Rosenfeld K, Razvi S, Walsh K, Symes J. Clinical evidence of angiogenesis after arterial gene transfer of phVEGF165 in patient with ischemic limb. *Lancet* 1996; 348: 370-4.
2. Baumgartner I, Pieczek A, Manor O, Blair R, Kearney M, Walsh K, Isner JM. Constitutive expression of phVEGF165 after intramuscular gene transfer promotes collateral vessel development in patients with critical limb ischemia. *Circulation* 1998; 97: 1114-23.
3. Rajagopalan S, Trachtenberg J, Mohler ER, Olin J, McBride S, Pak R, Rasmussen H, Crystal R. Phase I study of direct administration of a replication deficient adenovirus vector containing the vascular endothelial growth factor cDNA (CI-1023) to patients with claudication. *Am J Cardiol* 2002; 90: 512-6.
4. Lederman RJ, Mendelsohn FO, Anderson RD, Saucedo JF, Tenaglia AN, Hermiller JB, Hillegass WB, Rocha-Singh K, Moon TE, Whitehouse MJ, Annex BH; TRAFFIC Investigators. Therapeutic angiogenesis with recombinant fibroblast growth factor-2 for intermittent claudication (the TRAFFIC study): a randomized trial. *Lancet* 2002; 359: 2053-8.
5. Rajagopalan S, Mohler ER, Lederman RJ, Mendelsohn FO, Saucedo JF, Goldman CK, Blebea J, Macko J, Kessler PD, Rasmussen HS, Annex BH. Regional angiogenesis with vascular endothelial growth factor in peripheral arterial disease: a phase II randomized double-blind, controlled study of adenoviral delivery of vascular endothelial growth factor 121 in patients with disabling intermittent claudication. *Circulation* 2003; 108: 1933-8.
6. Henry TD, for the AGENT-3 investigators. AGENT 3: Angiogenic gene therapy 3 trial- intracoronary administration of Ad.FGF-4 in patients with no revascularization options. Available at: www.medscape.com/viewarticle/491660
7. Autiero M, Luttun A, Tjwa M, Carmeliet P. Placental growth factor and its receptor, vascular endothelial growth factor receptor-1: novel targets for stimulation of ischemic tissue revascularization and inhibition of angiogenesis and inflammatory disorders. *J Thromb Haemost* 2003; 1: 1356-70.
8. van Royen N, Piek JJ, Legemate DA, Schaper W, Oskam J, Atasever B, Voskuil M, Ubbink D, Schirmer SH, Buschmann I, Bode C, Buschmann EE. Design of the START-trial: Stimulation of arteriogenesis using subcutaneous application of GM-CSF as a new treatment for peripheral vascular disease. A randomized, double-blind, placebo-controlled trial. *Vasc Med* 2003; 8: 191-6.

STATINS AND PAD – not only improved survival, but also better quality of life

Different studies have shown that hyperlipoproteinemia is a relevant risk factor for PAD. Hypercholesterolemia has been found in 45-59% of symptomatic PAD patients, and statins have exerted beneficial effects on cardiovascular and cerebrovascular outcome in patients with PAD. In the Heart Protection Study (HPS), PAD patients treated with simvastatin had a significant reduction in vascular events and revascularization. Five years of statin treatment prevents 70 major cardiovascular events in 1000 patients with PAD (1). However, studies specifying the outcome of the PAD itself are sparse. In a 5-year follow-up study in which hypercholesterolemia was treated by partial ileal bypass (POSCH study), the incidence of claudication was reduced to 19% in the surgically treated group vs. 33.6% in the control group and the effect was related to the decrease of serum cholesterol (by 23.3%) (2). Similarly, a 2-year follow-up study of 153

patients with femoral atherosclerosis treated with colestipol–niacin demonstrated decreased progression of femoral atherosclerosis (3). Subgroup analysis of the Scandinavian Simvastatin Survival Study (4S) showed a risk reduction of almost 38% in new or worsening intermittent claudication (4). Some studies also indicated that in addition of their lipolytic effect, statins may directly influence peripheral haemodynamics and improve functional outcomes of PAD patients. Subjects taking statins had a better 6-minute walk performance, faster walking capacity and a higher summary performance score (5). Mondillo and co-workers reported improvement of walking performance and symptoms of claudication in hypercholesterolemic patients with PAD during high dose therapy with simvastatin (6). Similarly, atorvastatin treatment (80mg/day for 12 months) improved the pain-free walking distance and community-based physical activity in patients with intermittent claudication (7). Thus, patients with claudication do not benefit from statin treatment only by a reduction of major vascular events but also by an improved lifestyle. However, these trials were rather small and their results need to be confirmed in larger studies.

References

1. Heart Protection Study Collaborative Group: MRC BHF Heart Protection Study of cholesterol lowering with simvastatin in 20536 high-risk individuals: a randomized placebo controlled trial. *Lancet* 2002; 360: 7-22.
2. Buchwald H, Varco RL, Matts JP et al. Effect of partial ileal bypass surgery on mortality and morbidity from coronary heart disease in patients with hypercholesterolemia. *N Engl J Med* 1990; 323: 946-55.
3. Blankerhorn DH, Azen SP, Grawford DW et al. Effects of colestipol-niacin therapy on human femoral atherosclerosis. *Circulation* 1991; 83: 438-47.
4. Pedersen TR, Kjekshus J, Pyörälä K et al. Effect of simvastatin on ischemic signs and symptoms in the Scandinavian simvastatin survival study. *Am J Cardiol* 1998; 81: 333-5.
5. McDermott MM, Guralnik JM, Greenland P et al. Statin use and leg functioning in patients with and without lower-extremity peripheral arterial disease. *Circulation* 2003; 107: 757-61.
6. Mondillo S, Ballo P, Barbati R, Guerrini, Ammaturo T, Agricola, E et al. Effects of simvastatin on walking performance and symptoms of intermittent claudication in hypercholesterolemic patients with peripheral vascular disease. *Am J Med* 2003; 114: 359-64.
7. Mohler ER, Hiatt WR, Creager MA for the Study Investigators. Cholesterol reduction with atorvastatin improves walking distance in patients with peripheral arterial disease. *Circulation* 2003; 108: 1481-6.

ENDOVASCULAR REPAIR OF ABDOMINAL AORTIC ANEURYSMS – safer, but not necessarily more effective than open surgical repair

In 2003 the American Association for Vascular Surgery and the Society for Vascular Surgery have stated in their joint guidelines on treatment of abdominal aortic aneurysms that endovascular aneurysm repair (EVAR) was most suitable for patients at increased risk for conventional surgical aneurysm repair – in view of EVAR's uncertain long-term durability and effectiveness, as well as the increased surveillance burden requiring yearly follow up by computer tomography (1). Also, there appeared to be no justification for changing the accepted size thresholds for intervention in most patients when EVAR was considered in comparison to open surgery (1). Are these recommendations still true after two randomized trials comparing open surgical repair vs. EVAR have been recently published (2, 3)? Both the EVAR trial-1 from the United Kingdom in 1082 randomized patients with aneurysms of at least 5.5 cm in diameter and

the Dutch DREAM trial in 345 randomized patients with aneurysms of at least 5 cm in diameter have found a substantial reduction in 30-day mortality with the endovascular approach, i.e., 1.6% vs. 4.6% in EVAR trial-1 and 1.2% vs., 4.6% in the DREAM trial (2, 3). However, a recent editorial in the New England Journal of Medicine warns against the conclusion that endovascular repair is preferable to open repair (4). Operative morbidity and mortality rates represent only one half of the risk-benefit equation, and the two strategies can not be compared without considering subsequent events and reinterventions (4). Recent reports from the European EUROSTAR registry (5) and from the Cleveland Clinic (6) have raised concerns about long-term results of EVAR in large aneurysms. The 4-year post-EVAR rupture rate in the EUROSTAR registry was 10% in aneurysms measuring at least 6.5 cm in diameter as compared to 2% for smaller aneurysms (5), and in the Cleveland Clinic series 6.1% of patients with aneurysms measuring at least 5.5 cm died after 2 years because of aneurysm-related causes in comparison to 1.5% of patients with aneurysms measuring less than 5.5 cm (6). These findings are disturbing, because large surgical trials have not found any benefit of repairing aneurysms smaller than 5.5 cm (1). It is therefore not clear whether EVAR is any better than surveillance in patients with smaller aneurysms. Until long-term outcomes of EVAR are available, it would seem unwise to change the guidelines for clinical practice (1).

References

1. Brewster DC, Cronenwett JL, Hallert JW, Johnston KW, Krupski WC, Matsumura JS. Guidelines for the treatment of abdominal aortic aneurysms. Report on a subcommittee of the Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery. *J Vasc Surg* 2003; 37: 1106-17.
2. Greenhalgh RM; Brown LC, Kwong GP, Powell JT, Thompson SG. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised, controlled trial. *Lancet* 2004; 364: 843-8.
3. Prinssen M, Verhoeven ELG, Buth J, Cuypers P, van Sambeek MRHM, Balm R, Buskens E, Grobbee DE, Blankensteijn JD, for the Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial Group. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2004; 351: 1607-18.
4. Lederle FA. Abdominal aortic aneurysm – open versus endovascular repair. *N Engl J Med* 2004; 351: 1677-9.
5. Peppelenbosch N, Buth J, Harris PL, van Marrewijk C, Fransen G. Diameter of abdominal aortic aneurysm repair: does size matter? A report from the EUROSTAR. *J Vasc Surg* 2004; 39: 288-97.
6. Ouriel K, Srivastava SD, Sarac TP, O'Hara PJ, Lyden SP, Greenberg RK, Clair DG, Sampram E, Butler B. Disparate outcome after endovascular treatment of small versus large abdominal aortic aneurysm. *J Vasc Surg* 2003; 37: 1206-12.

CAROTID ANGIOPLASTY AND STENTING – at least not inferior to carotid

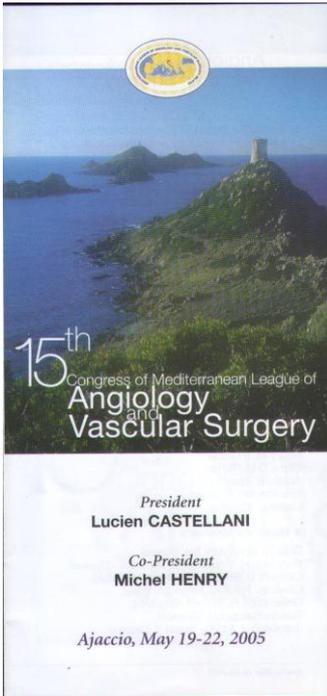
endarterectomy

The role of surgical endarterectomy in managing carotid artery stenosis is well established after the European (ECST) and North American (NASCET) carotid surgery trials have demonstrated long-term benefits for symptomatic patients with internal carotid narrowing (1, 2), and after a clear long-term benefit has been found in asymptomatic patients with severe stenosis after endarterectomy vs. medical treatment in the ACAS and the more recent ACST trials (3, 4). The perioperative risk of adverse events, i.e., stroke or death, must be less than 6% in symptomatic patients and less than 3% in asymptomatic patients for a favorable risk-to-benefit

ratio (5). In spite of the rapid growth in numbers of carotid angioplasty and stenting (CAS) for carotid artery stenosis, many surgeons are still skeptical of the procedure. The main question remains whether reducing arterial narrowing by CAS is as effective as surgically removing the entire atherosclerotic plaque in preventing arterial-to-arterial embolism, which is the main cause of carotid stenosis-related strokes. There is already some encouraging long-term data on the efficacy of CAS, and the early complication rate has been substantially reduced in 5 years, especially with wide-spread use of cerebral protection devices (6). The recently published 1-year results of the randomized SAPPHERE trial in high-risk patients have shown significantly fewer major cardiovascular events (death, stroke or myocardial infarction within 30 days after the intervention, or death or ipsilateral stroke between 31 days and 1 year) with CAS than with endarterectomy, i.e., 12.2% vs. 20.1% (7). The difference in the composite end-point was due mainly to the higher incidence of non-Q-wave myocardial infarctions in the endarterectomy group, but non-inferiority of CAS vs. endarterectomy has been firmly established in high-risk patients (7). Large scale, multicentre trials with longer follow-up have already been initiated and are expected to further clarify the role of CAS, especially in low-surgical-risk patients.

References

1. European Carotid Surgery Trialists' Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99 %) or with mild (0-29%) carotid stenosis. *Lancet* 1991; 337: 1235-43.
2. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high grade carotid stenosis. *N Engl J Med* 1991; 325: 445-53.
3. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. *JAMA* 1995; 273: 1421-8.
4. MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet* 2004; 363: 1491-502.
5. A multidisciplinary consensus statement from the Ad Hoc Committee, American Heart Association. Guidelines for carotid endarterectomy. *Circulation* 1995; 91: 566-79.
6. Roubin GS, New G, Iyer SS, Vitek JJ, Al-Mubarak N, Liu MW, Yadav J, Gomez C, Kuntz RE. Immediate and late clinical outcomes of carotid artery stenting in patients with symptomatic and asymptomatic carotid artery stenosis: a 5-year prospective analysis. *Circulation* 2001; 103: 532-7.
7. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, Bajwa TK, Whitlow P, Strickman NE, Jaff MR, Popma JJ, Snead DB, Cutlip DE, Firth BG, Ouriel K, for the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004; 351: 1493-501.



Preliminary announcement of the 15th MLAVS Congress

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Fig 1. Palermo-Sicily
Panoramic view

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NEWS IN ANGIOLOGY AND VASCULAR SURGERY IN THE MEDITERRANEAN REGION

The 15th Mediterranean Congress of Angiology and Vascular Surgery

took place in the Convention Centre of Hotel Florio in Palermo, Sicily. This region is well known as the cradle of ancient Hellenistic and Roman civilisations. The scientific programme of the Congress continued the tradition of previous MLAVS Congresses. It was composed of Round Tables, Lectures, Joint Symposia with other Italian and International Societies, Oral Presentations, Posters and Workshops. The sequence of events was as follows:

Friday (23/9/05)

The opening Ceremony took place in the Palazzo Dei Normanni in Palermo (Fig 2)



Fig 2: Palazzo Dei Normanni

After the welcome addresses given by the President of the Congress Prof S. Novo, the President of the Sicilian Parliament, the President of the Sicilian Region, the Rector Magnificus of the University of Palermo and the Director of the University Hospital "P. Giaccone" of Palermo, two **Opening Lectures** were delivered:

"Interventional vascular medicine: present status and future developments" (N. Kipshidze) and "European pioneers in Angiology

and Vascular Surgery" (N. Angelides).



Fig 3: N. Angelides, MLAVS Secretary General receiving an honorary plaque from President S. Novo.

A welcome Reception brought to an end the first day of the Congress.

Saturday (24/9/05)

The **Joint symposium** (MLAVS/ and the Working Group on Peripheral Circulation) was presented under the title "Atherosclerosis: systemic disease -systemic approach".

"Are atherogenetic mechanisms and morphology of atherosclerotic lesions identical in different locations?" was analysed first by A. Blinc. This, was followed by the "Diagnostic approach to a patient with suspicion of multifocal disease" by S. Novo, and the "Risk for cardiovascular events in multifocal arterial disease" by P. Poredos. Finally, this entity was closed by "the preventing measures according to the location of atherosclerotic process" by J. Lekakis. The next **keynote lecture** dealt with "Cell therapy and angiogenesis for



Fig 4: Evaluating Jacobson's prize

peripheral vascular diseases” by N. Kipshidze, and was followed by another **lecture** (F. Violi) under the title “Possible usage of hypocholesterolemic therapy in patients with coronary syndrome”. The next **symposium** dealt with “The advances in interventional cardiology: the role of IIb/IIIa glycoprotein inhibitors”. In this symposium “Indications and results of carotid stenting” were analysed by S. Tolaro, “Wall healing and arterial remodelling after carotid stenting” by H. Ehriger and “Is primary PTCA the best choice for patients with acute coronary syndromes?” by E. Hoffmann and M. Benedetto. These, were followed by “The role of GPIIb/IIIa inhibitors during PCI” (D. Ardissino) and “Elective PTCA for coronary disease in multifocal atherosclerosis” (C. Indolfi). Then, two **lectures**: “Intra-abdominal adiposity as a major cause of cardiometabolic risk” (D. Vanuzzo) and “Contemporary approach to the hemolymphatic malformations” (B.B. Lee) brought as to the next **Joint Symposium** (MLAVS/European Group of Lymphology) under the title “Modern strategies in lymphoedema management” E. Fulcheri, W. Olszewski, S. Michelini, C. Campisi, K. Benda and G. Thilbaut gave an intensive analysis on the prevention of primary and secondary lymphoedema, the techniques of lymphatic microsurgical operations and their long term outcome as well as the rehabilitation projects and monitoring of patients suffering from lymphoedema.



Fig 5: The Palermo “Acropolis”

This symposium was followed by a **keynote lecture** delivered by A. Markel under the title “The natural history of venous thrombosis”. The last **symposium** of the day was under the title “Management of vascular malformations and presented by R. Mattassi, B.B. Lee, F. Stillo, and C.M. Philip, while the last **keynote lecture** dealt with the “Development of stem varicose veins” and was presented by K. Roztocil.

Sunday (25/9/05)

The third day of the Congress started with a **symposium** on “The diagnosis and treatment of pulmonary arterial hypertension”. P. Mikus, A. Fijalkowsk, A. Manes, and N. Galie analysed the matter from the pathophysiological, diagnostic, and therapeutical view. A **keynote lecture** by P. Prandoni followed under the title “Emerging strategies for the treatment of venous thromboembolism”. A **symposium** (MLAVS/Working Group in Peripheral Circulation) was then presented under the title “Indicators of peripheral atherosclerosis and their clinical relevance”. First, M. Sabonic gave an analysis on “Circulating markers of endothelial dysfunction”. F. Cosentino analysed “Endothelial dysfunction” and P. Poredos “Intima-media thickness”

Finally, C Vlachopoulos gave an analysis on “Arterial stiffness and its clinical relevance”.



Fig 6: Narrow roads in old Palermo

Another **symposium**, dealing with “Update on treatment of aortic aneurysms” followed. In this symposium, R. Abbate gave an analysis on “Pathophysiology of aortic aneurysms”. G. Ruvolo and K. Fattouch analysed the “Treatment of ascending aortic aneurysms with or without aortic replacement” and N. Angelides the “Management of aortic aneurysms above and below the diaphragm” Then, P. Kalman gave an analysis on “Aortic reconstruction for complex indications” and G. Deriu dealt with the “Evolution of treatment of AAA”. “Endovascular management: a new option for the management of vascular disease” was the title of the next **symposium**. M. Henry tried to give an answer to the question “Is carotid angioplasty and stenting becoming the gold

standard treatment of a carotid stenosis?” Then, E. Bastounis spoke about “Aortic aneurysms” in general and P. Kalman about “Intervention for mesenteric occlusive disease: open intervention versus endovascular”. Finally, B. B. Lee gave an analysis on “Vascular malformations”. Then an interesting **Keynote Lecture** under the title “Proposal for European observatory of vascular disease epidemiology and care” was presented by F. A. Alleart and M. Cazaubon



Fig 7: Medieval buildings in Palermo

The final **joint symposium** of the day (MLAVS/European Working Group on Venous Classification), dealt with “CEAP: a critical review”. P. L. Antignani analysed the “New CEAP classification” and A. Cornu-Thenard “The computerized venous registry on the CEAP in daily practice”. Then, Ch. Liapis gave an analysis on “CEAP classification and surgery of CVI” while P. Poredos dealt with the “Use of CEAP in the management of venous Ulcers”. Finally J. F. Uhl reported on “Epidemiological studies using CVR”.

Monday (26/9/05)

The last day of the Congress started

with a **joint symposium** (MLAVS/ International Academy of Clinical and Applied Thrombosis) under the title “Are we on the right track with new drugs in the management of thrombosis and vascular disorders?” This interesting symposium was split in two parts:



Fig 8: The Prizes’ winners with Prof Strano, Novo and Angelides

The first part started with a lecture by J. Fareed “Are new drugs ready for prime time?” This was followed by a lecture on “Synthetic heparins Fondaparinux and Idraparinux” (J. Walenga), and another one on “Bioheparins as new anticoagulants” (U. Cornelli). Finally, B. Kaiser closed part 1 with a lecture on “Antithrombin and anti-Xa drugs”. **The second part** started with a lecture by S. Coccheri on “Defibrotide and related agents” followed by another on “Psychiatric comorbidity of heart disease: antiplatelet drug effects”. Then J. Fareed talked about “Genetic antithrombotic drugs” and finally E. Kalodiki presented “IUA consensus on the management of thrombosis”. The **final symposium** of the Congress had the title “From angioplasty to stent and eluting stents: advances and controversies in interventional therapy” P.G. Settembrini presented the “Early and late results of carotid

endarterectomy” followed by a lecture (N. Angelides) under the title “Is carotid intervention before coronary by-pass grafting mandatory?”



Fig 9: Medieval buildings in Palermo

Then, C. Tambrino presented the “Developments in drug eluting coronary stents”, A. Stella “The place of PTA in the treatment of peripheral arterial disease”, and J. Fernandes the final topic “Is PTA/stenting the first option for proximal aortoiliac stenosing disease?”

IASACO, IUA, and MLAVS Prizes

Three separate sessions were organized for the three prizes For the IASACO prize a committee composed by A. Strano as President and C. Allegra, A. Schriger and J. Walenga as members evaluated the oral presentations.

A second committee composed by S. Novo as president and B. B. Lee, H. Rieger and K. Rotzocil as members evaluated the oral presentations for the IUA prize. Finally, a third committee composed by N. Angelides as president and L. Castellani, C. Deriu and A. Tripolitis as members evaluated the oral presentations for the Jacobson’s-MLAVS Prize.

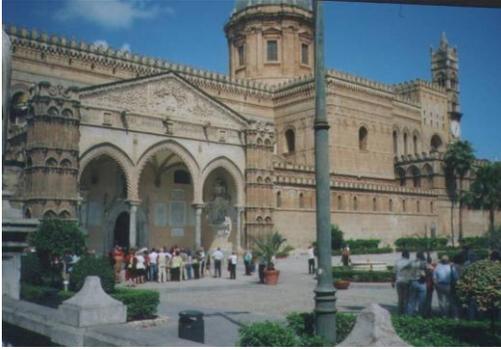


Fig 10: The cathedral of Palermo

Opening Lecture at the 15th MLAVS Congress: “European Pioneers in Vascular Surgery and Angiology in the 20th Century”, by N. Angelides.

Although it is nearly 200 years since vascular surgery was transformed by John Hunter from a terrifying craft to a positive scientific success, there have been long stagnant periods during which little progress could be seen. Arteriography and the advent of practical grafting techniques led in the early 1950s to a golden age of consolidation and widespread achievement, at the height of which further progress was difficult to foresee. This period ended in 1967 with the arrival of coronary artery by-pass surgery and the Doppler flow velocity apparatus. Since then, hundreds of thousands of patients had experienced the benefits of these two advances. (Rene G. Favaloro, was the first to perform an aorto-coronary by-pass in 1967 and D.E. Strandness, was the pioneer in vascular ultrasonography).

At the end of the 19th century and the beginning of the 20th, experiments were carried out all over the world on vascular suturing. The French School had the greatest success in the research. Alexis Carrel and Rene Leriche in Lyon were the first to

evolve modern techniques of vascular anastomoses. Alexis Carrel could not find satisfactory working conditions in Europe and emigrated, first to Canada and then to Chicago. In 1912 he was awarded the Nobel Prize for medicine for his work on vascular suturing and anastomoses. Rene Leriche created a School of vascular Surgery in Strasbourg. Members of this School were my teacher Prof Christeas, Prof Dos Sandos, Prof De Bakey and Prof Jean Kunlin.

Angiography was developed in Portugal. Moniz performed the 1st cerebral angiogram in Lisbon in 1927. Reynaldo Cid dos Santos performed the 1st aortogram in the same city in 1929. J. Kinmonth, Professor of surgery at St. Thomas' hospital, was a pioneer in the study of lymphatic diseases and invented peripheral lymphangiography.

Heparin was discovered in America by William Howell and Jay McLean (1925). However, it was manufactured in crystalline form by Fischer and Schmitzin in Copenhagen in 1933. Finally, it was used by Crafood in Stockholm in 1937 to treat patients with DVT. The first endarterectomy of the superficial femoral artery was carried out under local anaesthesia in Lisbon in 1946, by Jean Cid dos Santos. The 1st fem-pop by-pass graft was performed by Jean Kunlin in Paris in 1948. It is worthwhile to mention that Rene Leriche, the teacher of Kunlin, was sceptical about the idea of a venous by-pass graft, because he believed that arterial pressure could rupture the vein. For this reason Kunlin waited until Leriche was out of town before operating upon his 1st patient, who had critical limb

ischaemia and impending gangrene! Jacques Oudot, again in France, performed the first inlay aortic graft in 1950, using an aortic allograft from a young victim of an accident. The first operation to repair an abdominal aortic aneurysm was carried out in 1952 by another Frenchman, Charles Dubost. He performed the operation using a thoracic aortic allograft from a young accident victim.

My teacher, Felix Eastcott, is credited with the first reported carotid reconstruction for recurrent TIAs in London, in 1954. However, it was Michael DeBakey who carried out a similar operation just before Eastcott in Huston, Texas.



Fig 11: R. Leriche School of Vascular Surgery. Members of the service were DeBakey, N. Christeas, Dos Sandos, and J. Kunlin (all in the front row)

The well known Hippocrates aphorism "*ocosa farmaca uk iite sidiros iite = when drugs do not help then surgery helps*", which was an axiom for centuries, seems suddenly to loose its real value, as we move into the era of endovascular surgery. The invention of an effective balloon for arterial dilatation by Andreas Gruntzing

opens the gates for endovascular repair. Gruntzing carried out the first femoral and iliac angioplasties with a balloon catheter in 1972 and the first coronary angioplasty in 1977, in Zurich. He also performed the first renal angioplasty with Felix Mahler in Bern, again in 1977. Juan Parodi performed the first endovascular repair of an abdominal aortic aneurysm in Buenos Aires, in 1990, using a straight graft, stented at the proximal end only. However, the first modular intra-aortic stent/graft was introduced by Claude Mialbe. Also, J. Volmar, a pioneer German vascular surgeon, in Ulm, invented vascular endoscopy.

While contributions of physicians and scientists from other continents merit recognition, Europe can claim to have been the cradle of Vascular Surgery. Fundamental principles were established throughout the twentieth century, by the end of which vascular practice has evolved into a well defined speciality with its own specific diagnostic and therapeutic techniques Today, advances in the management of vascular disease continue to progress at an accelerating pace. The modern vascular specialist must have a wide range of skills at his command bridging traditional divides between the conventional surgical, medical and radiological specialities. The need to respond to these changes and ensure that vascular patients in Europe continue to have access to the highest possible standards of care, gave birth to the European Board of Vascular Surgery (EBVS)- associated with the Section of General Surgery of the UEMS in 1993, in Edinburgh. On the 15th of October 2004, in Lisbon, the UEMS

Management Council decided that Vascular Surgery should become a separate Specialist Section. What is the meaning of this independent Board? In the European Union, we will now be in a stronger position to support our claim of having Vascular Surgery as a main independent speciality, listed as such in the forthcoming Directive on Professional Qualifications. At national level, it will be of the utmost importance for those countries where Vascular Surgery is not a monospeciality to reach that goal. It will finally help our Colleagues across the Atlantic to achieve an independent Board of Vascular Surgery. To conclude, everything is always a matter of team work.

Site of future IUA World and European Chapter Meetings.

22d World Congress: 24-28 June 2006
Lisbon, Portugal. Organizer: Prof. J. Fernandes
23d World Congress: 2008, Greece.
Organizer: Prof. E. Bastounis
24th World Congress: 2010, Argentina.
Organizer: Prof. R. Simkin

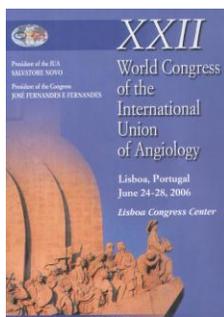


Fig 12: Second announcement for next IUA World Congress in 2006

17th Congress of the European Chapter of the IUA-EUROSHAP
26-29 April 2007, Nicosia, Cyprus.

Organizer: Prof. N. Angelides.

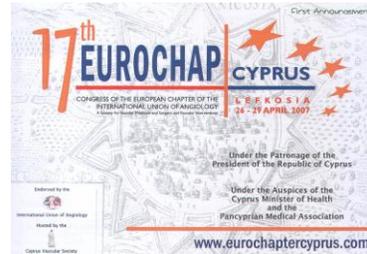


Fig 13: First announcement for the next EUROCHAP in 2007

Future MLAVS Congresses

*The 16th MLAVS Congress will take place in Heraklion, Crete, 9-12 June 2006 and will be organised by Prof. Ch. Liapis.
*The 17th MLAVS Congress will take Place in Mallorca in 2007 and will be organised by Prof V. Riambau.

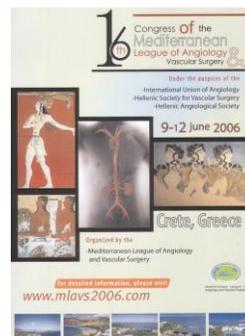


Fig 14: First announcement for next MLAVS Congress in 2006

New Books

The “Volume on Vascular Surgery: European Manual of Medicine” (Springer-Verlag) – In press

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