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### **AIMS AND SCOPE**

*Phlebolymphology* is an international scientific journal entirely devoted to venous disease.

The aim of *Phlebolymphology* is to provide doctors with updated and interesting information on phlebology and lymphology written by wellknown specialists from different countries worldwide.

*Phlebolymphology* is scientifically supported by a prestigious editorial board.

*Phlebolymphology* has been published four times per year since 1994, and, thanks to its high scientific level, was included in the EMBASE database in 1998.

*Phlebolymphology* is made up of several sections: editorial, articles on phlebology and lymphology, news, review, and congress calendar.

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## **EDITORIAL**

he American Chapter Meeting of the Union Internationale de Phlébologie (UIP) was held in San Diego from August 27 to 30, 2003, under the aegis of the American College of Phlebology and with the participation of many other scientific societies from all over the World. On this occasion, The American Venous Forum held its symposium on "Guidelines on the Management of Venous

Disorders" (see part 6 of the present report). Many countries were represented, and this was a major opportunity to compare experiences from different continents. In contrast to previous meetings, no more than four sessions ran in parallel, so that more time could be given to each topic. Attention was focused on new techniques that are in rapid progression, and that will drastically change our views and habits in the phlebology field. In particular, the

increasing use of foam sclerotherapy and various endovenous closure procedures, rather than previously accepted surgical stripping, is becoming evident. These less invasive methods that allow extension of treatment to older people were thoroughly explored by different teams who shared their interesting experience with all attendees during the congress. Also, the results of large-scale epidemiological studies, such as the Bonn Vein study, the Sao Paulo study, and the fourth part of the Bochum study, were presented. Most of these studies used the CEAP classification that is now universally adopted and allowed comparison. We learned of important findings in the schoolchildren of Bochum, particularly that detection of reflux usually precedes the clinical appearance of varicose veins, and that early detection of reflux in superficial veins may offer opportunities for preventive measures. New insight into the pathophysiology of venous disease was provided by different teams. The central role of the venous endothelium has been highlighted, and changes in endothelial activity of patients with venous disease have been observed. Effective pharmacological agents have been found to stabilize the endothelial cells at the level of large veins, and even, in the case of one of the most representative

> phlebotropic drugs, to act at the level of the capillary endothelium, thus accelerating leg ulcer healing. Other sessions dealt with risk factors for venous disease, compression therapy, and also superficial and deep venous disease. A special mention is to be given to the UIP initiatives and awards, with the presentation of different projects and research works. Prof Schultz - Ehrenburgh was awarded the first prize for scientific studies by the American College of

Phlebology for his papers on the Bochum study (I to IV).

As President of the UIP, I find it of utmost importance that all the scientific presentations of the San Diego congress remain available, not only for those who attended all sessions, but also for those who were not present. In this special issue, much information will be available on the many presentations, thanks to the report by the team of the Medical Reporters' Academy, initiated by Servier International.

This team, chaired by Andrew Nicolaides, has selected a large amount of information. I do welcome this excellent initiative, and I wish you interesting reading.

#### **Professor Claudio ALLEGRA**

President of the Union Internationale de Phlébologie



Professor Claudio ALLEGRA



## PREFACE

his report from the American Chapter Meeting of the Union Internationale de Phlébologie, San Diego, has been prepared by the members of the Medical Reporters' Academy (MRA). This group, composed of young medical doctors selected from different European countries, was created and sponsored by Servier 7 years ago. Since then, the MRA group has been attending major international congresses in Phlebology and Angiology in order to keep specialists all over the world fully informed of recent developments in the field. Each day of the congress, all sessions are covered, and the team select the best information at evening meetings. This report is not intended to be an exhaustive account of each presentation, but much more to provide highlights on what is considered to be new in Phlebology. I wish you enjoyable reading.



Professor A. N. NICOLAIDES

### Prof A. N. Nicolaides

Chairman of the MRA Chairman and Medical Director, The Cyprus Institute of Neurology and Genetics Emeritus Professor of Vascular Surgery, Imperial College of Science, Technology and Medicine, London Past President of the International Union of Angiology

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Part 1



# **NEW TECHNIQUES**

Classical operations for varicose veins (VV) are performed less and less. The increasing use of foam sclerotherapy and various endovenous closure devices (endovenous laser therapy (EVLT), VNUS® radiofrequency closure) rather than classical surgical management is becoming evident. These less invasive therapies allow treatment of older people who

in the past would have been treated only by compression. Prof J. J. Bergan (USA) pointed out that with these techniques the classical surgical approach to the saphenofemoral junction in VV disease is only necessary in cases with venous aneurysms exceeding 2 cm in diameter at the level of the preterminal valve in the junction.

## LASER AND RF CLOSURE TREATMENTS FOR VEIN DISEASE

Moderators: L. GRONDIN (Canada), N. SADICK (USA)

# 1320 nm endovenous laser treatment of the greater saphenous vein (GSV)

M. P. GOLDMAN (USA)

Nost papers on endovenous laser treatment (EVLT) describe the use of laser frequency of 810 nm or 980 nm. The chromophore of these frequencies is hemoglobin. The heat of the laser tip is approximately 1000° C, causing the blood to boil. This leads to pain and bruising, and may sometimes result in perforation of the vein wall.

The author of this paper describes his experience with a laser of 1320 nm on 50 patients with varicosities of the GSV. The higher frequency of the laser has water as its target structure therefore acting directly on the vein wall. Bruising and pain were significantly decreased compared with the other lasers used in that indication.

### Radiofrequency ablation of refluxing superficial and perforating veins using VNUS closure and transluminal occlusion of perforator veins

M. WHITELY (UK)

he author reported extensive experience on RF closure procedures in 1022 legs with varicose veins.

In contrast to other centers only treating GSV and SSV varicosities, veins treated were:

Primary reflux	804
Recurrence	218
Giacomini	51
Medial or lateral side branches	235
Legs with incompetent perforators	411

Alfentanyl preventing venospasm was used in order to ascertain complete closure by the RF treatment. Local anesthesia can produce a venospasm mimicking successful therapy. No local anesthetics were used, as general anesthesia was necessary due to the apnea induced by the alfentanyl.

The excellent results seem to warrant this method. The rates of complete occlusion with resulting atrophy was as follows:

l year	216/217	99.5%
2 years	106/106	100%
3 years	26/26	100%

Clinical recurrence rates were low and due to de novo reflux or missed side branches. Larger numbers and long-term follow up are needed.

## **ENDOVENOUS OCCLUSION TECHNIQUES**

Chairpersons: T. PROEBSTLE (Germany), S. E. ZIMMET (USA) Speakers: S. M. DOSICK (USA), R.F. MERCHANT (USA), K. L. TODD, III (USA), T. PROEBSTLE (Germany), R. MILLERET (France), R. J. MIN (USA), A. TZILINIS (USA)

The session was devoted to various aspects of radiofrequency ablation (RFA) and endovenous laser treatment (EVLT).

S. M. Dosick compared RFA in treatment patients older than 70 years with that in patients younger than 70 years. He did not find significant differences in the postoperative and rehabilitation period in this group (35 patients, 41 limbs) in comparison with patients <70 years (386 patients, 449 limbs). Forty percent of patients of the group >70 years had active/nonactive ulcers. All ulcers were healed by 3 months after operation. The author concluded that RFA can be a safe method for treatment of older patients with intercurrent pathology.

R. F. Merchant successfully performed RFA for treatment of 10 patients with insufficiency of the short saphenous vein (SSV). Successful, complete closure of the SSV was achieved in 10/10 (100%). No complications occurred. The author concluded that RFA can be use for safe treatment of SSV reflux.

Different types of diode lasers (810 nm, 940 nm, 980 nm) have been used for EVLT.

K. L. Todd presented a series of patients with 386 greater saphenous veins (GSV) treated with EVLT. All patients were evaluated with duplex ultrasound at intervals varying from 3 to 12 months;

377 GSV had no reflux postoperatively. The author concluded that EVLT is an effective method for long-term venous ablation.

R. J. Min presented the follow-up results of EVLT in 610 patients (701 limbs). There were GSV (566 limbs), SSV (65 limbs) and anterior-lateral tributaries (70 limbs). The 2-year follow-up demonstrated a recurrence rate of less 7%.

T. Proebstle presented the detailed description of EVLT technique and mechanism of the GSV obliteration. The author had experience of EVLT in 85 patients (104 GSV) with CVI clinical stage C 2 to 6. He demonstrated that endovenous laser produces small steam bubbles which mediated heat injury to the endothelium with secondary thrombotic occlusion. The author discussed how different endovenous methods influence vessel shrinking and thrombus formation (*Table I*).

In 8.6% (9 limbs) recanalization of (4.8%-complete and 4.8%-proximal) were found during 12 – month follow-up with duplex examination. All these patients required further treatment by high ligation and stripping.

R. Milleret compared the results of various methods of the endovenous treatment of incompetent GSV (RFA, EVLT and catheter-delivered foam sclero-therapy *(Table II)*.

Table I. Influence of the different endovenous methods on the vessel shrinking and thrombus formation		
Method Vessel shrinking Thrombus formation		
RFA	+++	+
EVLT	+	++
Sclerotherapy	-	+++

Complete disappearance of the vein lumen was achieved in 8/25 cases with RFA and 4/25 cases with EVLT.

A. Tzilinis used a Quality of Life (QOL) questionnaire for an estimation of the RFA results. This specific questionnaire was developed by Launois (1996) and has been successfully validated in the well known RELIEF study. A. Tzilinis concluded that RFA of the incompetent GSV significantly improves patient's QOL. The average preoperative score was 49+15, decreasing postoperatively to 29+10, for a 41% improvement (P<0.001).

Table II. Results of application of RFA, EVLT and catheter foam sclerotherapy				
Procedure used	Diameter of the GSV (mm)			
	Before procedure1 month after1 year after			
RFA	7.09	4.27	2.43	
EVLT	6.70	4.38	2.78	
Catheter sclerotherapy	6.81	4.79	2.40	

## **ADVANCES IN MICROFOAM THERAPY**

Chairpersons: J. J. Bergan (USA), R. A. Weiss (USA)

### Review of the use of foam

A. FRULLINI (Italy)

**S**clerosing foams (SF) are mixtures of gas and liquid solution with surfactant properties, affording full control of drug concentration inside the vein and contact time with the endothelium. Cabrera proposed the use of a microfoam of sodium tetradecyl sulfate and polidocanol for sclerotherapy in 1993. Many authors subsequently reported different methods for foam production. Sclerosing foam is characterized in part by the following parameters:

- type and concentration of sclerosant
- type of gas, ratio of liquid to gas

- additional nonactive substances
- the method of preparation
- the time after processing
- bubble size distribution.

Now, several pharmaceutical companies have become interested in foam. For example, a British company is developing a fully characterized microfoam (Varisolve<sup>™</sup> - Provensis, UK) made to approved pharmaceutical standards.

### The science of microfoam

T. HARMAN (UK)

A microfoam has a number of unique physical properties. Bubble size, fluid-to-gas ratio, and foam breakdown rate are all highly important. New measurement techniques were developed to define the essential differences between microfoams, foams, and froths, depending on the diameter of bubbles:

- froth >500 mm
- foam >300-500 μ
- microfoam <250 μ

Microfoams are characterized by:

- density
- stability
- bubble size distribution.

Density is controlled by the ratio of fluid to gas. Stability is dependent on viscosity, dissolved gas, temperature, and bubble homogeneity. The most important criterion for microfoam stability is half separation time (HST). HST is the time taken for half the liquid component of the microfoam to separate from the gas. Bubble size distribution measurement is complex and must also be performed quickly. Further examination of properties of microfoam intended for medical purposes is necessary.

### Safety of intravenous foamed sclerosants

D. WRIGHT (UK)

**S**uperficial thigh veins of dogs were injected with 1% polidocanol microfoam, 5 mL/sec. Pulmonary artery pressure (PAP), mean systemic arterial pressure (MAP), EKG, transesophageal echo-ultrasound, O<sub>2</sub> saturation, and tidal CO<sub>2</sub> were continuously recorded. Cardiac output and pulmonary and peripheral resistance were measured. Three dosage

models were investigated (single, multiple with fixed interval, and multiple with variable interval). A significant, rapid, and dose-dependent rise in PAP and fall in MAP followed injections >10 mL. Thus, sclerosant microfoam injected in dogs caused significant pulmonary hypertension and depressed cardiopulmonary function.

### European randomized controlled trial of Varisolve<sup>®</sup> PD microfoam compared with alternative therapy in management of moderate-to-severe varicose veins: preliminary results

D. WRIGHT (UK)

**S**even countries (France, Belgium, Sweden, Germany, Netherland, Italy, UK) took part in the prospective study of the clinical application Varisolve<sup>®</sup> foam. Aims of this study were:

- to demonstrate the safety and efficacy of Varisolve<sup>®</sup> in the treatment of moderate-to-severe varicose veins
- to compare the safety and efficacy of Varisolve<sup>®</sup> using 1% polidocanol with best alternative conventional treatment for varicose veins (surgery or sclerotherapy).

Varisolve<sup>®</sup> microfoam was injected under ultrasound control into incompetent trunk veins. Posttreatment follow-up evaluation included duplex ultrasound, photography, and Launois's (1996) Quality of Life questionnaires. The end point was the elimination of reflux and occlusion of the affected trunk vein. For the purposes of the study 658 patients were recruited. They were divided into three groups:

- 654 patients treated
  - 435 Varisolve®
  - -125 sclerotherapy
  - 94 surgery
- Age mean 50.0 (SD 12.2) range 19-75
- Sex 68.2 female, surgery cohort 63%, sclerotherapy 71%

• Great sapherous vein (GSV), 83.3% mean diameter 7.44 mm

- Short sapherous vein (SSV), 19.5% mean diameter 6.55 mm
- Recurrent varicose veins, 13.6%

There were 14 related adverse events (Table I).

### Table I. Adverse event

### Deep venous thrombosis (DVT)

- -11 (2.5%) Varisolve®
- 1 (0.8%) sclerotherapy
- 2 (2.1%) surgery

### DVT 11 in Varisolve®

- 2 symptomatic: one popliteal following
- SSV and one not related
- 2 popliteal and calf veins
- 3 isolated muscular calf vein thrombi
- 4 extension of sclerosis with thrombus beyond the SFJ

### No pulmonary emboli

The elimination of reflux was achieved during 3 months' follow-up in all treatment groups. Thus, Varisolve® microfoam has similar short-term efficacy to flush ligation and stripping. Sclerotherapy, while least invasive, was also least effective.

# French experience with Varisolve® PD microfoam in the management of moderate to severe varicose veins

J. P. GOBIN (France)

he study included 342 patients with greater (GSV) and/or short saphenous vein (SSV) incompetence, with moderate-to-severe varicosities. All patients were divided into two groups according to method of sclerotherapy (*Table I*).

The results of application of Varisolve<sup>®</sup> sclerotherapy were compared with liquid sclerotherapy *(Tables II, III, and IV)*. It was the preliminary conclusion that Varisolve <sup>®</sup> sclerotherapy provides high efficiency, little discomfort, and few complications.

Table I. Groups of patients			
		Foam sclerotherapy with Varisolve® (n=229)	Liquid sclerotherapy (113)
Age	Mean	50.8	50.0
	SD	12.4	12.0
	Range	19-75	20-74
Sex	Male	71 (31%)	32 (28.3%)
	Remale	158 (69%)	81 (71.7%)
CIVIQ	Mean	19.5	18.9
	SD	15.5	15.3

Table II. Occlusion and elimination of reflux during 3 months' follow-up			
	Varisolve <sup>®</sup> Liquid sclerotherapy		
GSV	153/157	69/72	
SSV	42/43	20/21	
GSV & SSV	3/3	1/1	
Recurrent	25/26	18/19	

Table III. Adverse events		
	Varisolve <sup>®</sup> n (%)	Sclerotherapy n (%)
DVT	1 (0.4)	1 (0.9)
Superficial thrombophlebitis	1 (0.4)	0
Pain in limb	70 (30.6)	28 (24.8)
Headache	7 (3.1)	7 (6.2)
Visual symptoms	2 (0.9)	2 (1.8)

Table IV. Number of injections		
Number of injections	Varisolve <sup>®</sup> (%)	Liquid sclerotherapy (%)
1	92.2	75.2
2	7.4	15.2
3	0.4	8.0
4	0	1.6

# Ultrasound-guided injection of polidocanol microfoam in the management of venous leg ulcers

J. CABRERA GARRIDO, A. BECERRA, M. COBO, C. GARRIDO, M. CABRERA Jr (Spain)

One hundred and seventy-one patients (180 limbs) with venous ulceration were treated. The mean age of patients was 58.5 years, and 8.33% of them were older than 75 years. The mean duration of the ulcers was 5.8 years. The reasons for ulceration were greater saphenous incompetence (147 limbs), deep venous reflux (55 limbs), and perforator vein incompetence (98 limbs). Ultrasound-guided

injection of polidocanol microfoam was performed in all cases for reducing venous hypertension. One hundred and sixty-three (90.6%) ulcers were healed over 3.7 years' follow-up (mean rate 2.7 months) without serious complications. There were 28 recurrences of ulcers in this group, which needed additional treatment.

## Testing foam made on-site for sclerosing varicose veins

S. SADOUN (France)

There are two tests for estimation of quality of the foam in vitro.

**Test A:** On a flat piece of glass, a drop of foam is deposited to calculate the time the foam return to a liquid form.

Test B: A drop of foam is deposited on an inclined

(15°) piece of glass: the time it takes to reach the bottom determines the foam's adhesiveness to the surface.

It is obvious that stability and adhesiveness lead to better results.

# Foam closure of the long saphenous vein: preliminary report

R. GONZALEZ ZEH (Chile)

wenty-eight patients (33 limbs) with long saphenous vein (LSV) incompetence were treated. Polidocanol 3% foam (10 cc per session) was injected into the LSV. Ultrasound duplex control was obligatory. Class I compression was used for 3 months.

There were no serious complications over 24 months' follow-up. Distal transient parasthesias were found in 6% of limbs. Eighty-five percent of LSVs were closed during 24 months' follow-up.

# Endoluminal therapy with echo-guided sclerosant foam: current situation after 30 years of experience

A. L. CABRERA GARRIDO, B. CABRERA NYST (Spain)

herapy with sclerosant foam of soluble gases and detergents offers four important advantages:

- Lower dose of sclerosant
- Increase tolerability to extravasation
- Accurate echographic control of application area
- Sclerosant agent and its action stay in situ.

There are more important principles of the effective and safe application of the foam-form sclerotherapy:

• An accurate and complete anatomohemodynamic venous map

- Formulations in accordance with objectives of sclerosant foaming agent
- Stable and consistent foam obtainable using special technical procedure
- Complete intervention on first session
- Ultrasound evolutionary short-term and medium-term monitoring for early detection and secondary treatment recurrences.
- Detailed list of essential technical instruments

# Microfoam ultrasound-guided sclerotherapy for varicose veins in a subgroup with diameter at the junction of >10 mm compared with a subgroup <10 mm

J. M. BARRETT, M. COLDMAN, B. ALLEN, A. OCKELFORD, K. JACOBSEN (New Zealand)

**S**ixteen legs with long saphenous veins (LSV) with a diameter at the junction of >10 mm (average diameter 12 mm) were compared with 97 LSVs with a diameter at the junction of <10 mm. Ultrasound-guided sclerotherapy (UGS) was performed in all cases. Patients were asked to complete a "quality of life" questionnaire by Launois (1996). Post-sclerotherapy examination included visual

and Duplex ultrasound assessment. Results of investigations are presented in *Table I*.

Patient satisfaction parameters were very similar for both groups. Thus, foam UGS sclerotherapy is equally effective for treatment of varicoses in LSV with diameter at the junction >10 mm.

Table I. Results of microfoam UGS sclerotherapy during 2-year follow-up		
Clinical parameter	D at the junction >10 mm	D at the junction <10 mm
Disappearance of the visible varicosities	94%	92%
Closure at the junction	69%	77%
Minimal flow	19%	20%
Persistent reflux	12%	4%
Number of treatments	2.8	2.15
Volume of foam	13.9 mL	8.37 mL

# Results of a European consensus meeting on the use of foam in sclerotherapy of varicose veins

F. X. BREU (USA), S. GUGGENBICHLER, E. RABE (Germany)

A European Consensus Meeting on the use of extemporary foams in sclerotherapy of varicose veins took place in Tegernsee, Bavaria, Germany in April 2003. The purpose of this meeting was to reach a consensus and come up with practical suggestions on foam sclerotherapy, including diagnosis, indications and contraindications, equipment, therapeutic strategies, application of sclerosing foam, efficacy, adverse events and complications, post-sclerotherapy treatment, etc.

More than 20 experts from different European countries actively discussed the subject. All participants agreed that the use of sclerosing foam is an appropriate procedure in the therapy of varicose veins. Sclerosing foam is a powerful tool in expert hands and in general more effective than the liquid form of sclerosants. It is necessary to have good skills in conventional liquid sclerotherapy before starting with foam sclerotherapy.

## FOAM SCLEROTHERAPY

Chairpersons: J. J. GUEX, (France), R. A. WEISS (USA)

## Aethoxysclerol foam obliteration of insufficient perforating veins in patients suffering from leg ulcers: a clinical recommendation

Z. RYBAK (Poland)

To assess the influence of elimination of venous reflux on the healing of leg ulcers, 40 patients were enrolled and divided into two groups randomized according to their age, sex, and the history of the disease, and treated with conservative treatment

for one group or by foam sclerotherapy for the other group.

The authors concluded that the obliteration of insufficient leg perforators increased the rate of healing in ulcers. Results are shown in *Table I*.

Table I. Comparative results between groups		
	Conservative treatment (compression, local debridement, pharmacotherapy)	Obliteration by means of 3% Aethoxysclerol foam
	20 patients	20 patients
Recovered after 6 months	9 patients	15 patients

# Echo-sclerotherapy of the greater saphenous vein by direct puncture using sclerosing foam

C. HAMEL-DESNOS, J. J. GUEX, P. DESNOS, et al (France)

The authors compared the efficacy of polidocanol foam versus liquid for echo-sclerotherapy of the greater saphenous vein by direct puncture. They tried to assess the reproducible evidence of the efficacy and the safety of this method.

After 2 years' follow-up the authors stated that in

order to avoid disappointment and accidents this technique requires knowledge of foam preparation, manipulation, and injection, as well as experience in conventional liquid sclerotherapy and venous echo-Doppler.

### Treatment of venous aneurysm with foam sclerotherapy

G. BELCARO, M. R. CESARONE (Italy), K. MYERS (Australia)

The authors reported the example of a 65-year old woman who complained of the existence of a lump located at the third, internal part of the left femoral fold. The lump was painless and easily obliterated by compression. Color duplex scanning showed a large cavity (4x4x6 cm) with venous flow visible. The authors performed two obliteration sessions (0 and 2 weeks) with the guidance of

ultrasound, by means of foaming agent. To avoid passage of sclerosing foam into the femoral vein, compression of the femoral vein was used. After 4 weeks the authors obtained a complete occlusion of the aneurysm which was confirmed 12 weeks later, and they hope that this method, never described before, will prove to be a good solution in the treatment of venous aneurysms.

## Treatment of severe CVI with sclerosant foam

J. J. BERGAN, L. V. MEKENAS (USA)

o assess the usefulness of foam sclerosant in treatment of CVI classes 4, 5 and 6, 30 limbs in 24 patients were enrolled in the study. Venous clinical severity (VCS) and the healing of the lesion were considered as end points.

The data are presented in Table II.

The authors consider the advantage of sclerotherapy with foamed sclerosant over compression therapy of severe CVI. Used early it can shorten treatment time.

Table II. Comparative results between groups		
Group 1 19 limbs in 15 patients	Group 2 11 limbs in 9 patients	Group 3 6 limbs, all failures of treatment in group 1
Compression	Compression + foamed sclerosant	Compression + foamed sclerosant
CEAP 5 – 3 limbs CEAP 6 – 16 limbs	CEAP 4 – 2 limbs CEAP 5 – 2 limbs CEAP 6 – 7 limbs	CEAP 5 – 1 limb CEAP 6 – 5 limbs
Seven limbs in 6 patients failed to heal with best medical care, six were reclassified as group 3	All ulcers healed VCS from 23.5 to 8.2	All ulcers healed VCS from 20.2 to 4.5

# Microfoam ultrasound - guided sclerotherapy for varicose veins in a subgroup with diameter at the junction >10 mm compared with a subgroup < 10 mm

J. M. BARRETT, M. P. GOLDMAN, B. ALLEN, et al (New Zealand)

The authors analyze the efficacy of ultrasoundguided sclerotherapy for varicose veins. By means of an improved foam-making technique, they

could reach 90% efficacy after the first injection. The diameter at the junction does not influence the final treatment results.

# Color duplex imaging and intraoperative assessment of terminal valve competence at the saphenofemoral junction

A. CAVEZZI, C. TARABINI, M. G. BARBONI, et al (Italy)

he results of a multicenter prospective comparative study (18 patients with varicose veins - C2-C5) were collected and analyzed. Preoperative data regarding greater saphenous vein incompetence without reflux at the terminal valve (TV) of the saphenofemoral junction (SFJ) were compared with intraoperative assessment of competence of the TV at SFJ. To assess possible blood reflux from deep veins through the SFJ the GSV 2 to 4 cm below the SFJ was cut off by the authors without

division of tributaries, and then the Valsalva maneuver and manual compression of iliac fossa were performed. Four out of 18 patients had slight reflux in the GSV stump. When the lower tributaries were disconnected, three out of those 4 still had reflux, and no reflux was observed when the upper tributaries were disconnected. These interesting findings can lead us to the conclusion that in the presence of competent TV, retrograde flow in GSV can derive from saphenous tributaries.

## **SCLEROTHERAPY**

### Moderators: M. P. GOLDMAN (USA), A. FRULLINI (Italy)

A randomized clinical trial comparing the effects of foam vs liquid formulas for sclerotherapy of primary varicose veins Perfluoropropane-filled albumin microspheres-sodium tetradecyl sulfate vs air-filled sodium tetradecyl sulfate for foam sclerotherapy of great saphenous vein incompetence

P. RAYMOND MARTIMBEAU (USA)

The author presented two studies with similar methodology in similar groups of patients. The first study compared liquid vs foam sodium tretradecyl sulfate (STS) in patients with varicose veins. The efficacy and the safety of the foam preparation were greater compared with the patients treated with the liquid formula. *(Table I)* 

group treated by perfluoropropane-filled albumin microspheres prior to injection of the STS foam in order to obtain a vein devoid of blood. The perfluoropropane-filled albumin microspheres – sodium tretradecyl sulfate preparation worked better concerning effectiveness and side effects.

In the second study a group treated with the foam preparation of STS 1% was compared with another

Table I - Treatment success after 1 year			
Liquid STS Foam STS			
Great saphenous vein	1.2%	44%	
Small saphenous vein	48%	84%	
Perforators	90%	96%	
Tributary	88%	100%	

### Foam echosclerotherapy of incompetent saphenous veins

L. GRONDIN (Canada)

he author described his work with a foam preparation on a basis of  $CO_2$  enabling him to use larger quantities (up to 25 cm3) of the therapeutic preparation.  $CO_2$  based foams have freater safety when compared with air-based foam, as  $CO_2$  is 20 times more soluble than air. It is therefore less likely to cause air embolism-related symptoms such as chest pain and transient ischemic attacks. These have been described as rare, but there are major side effects with air-based preparations, especially

when larger volumes are given. Foam preparations have been found to be superior to liquid sclerotherapy, especially in patients with recurrent varicose veins. The results of foam sclerotherapy were comparable to those of surgery at the 5-year follow up. *(Tables I, II)* 

Side effects were more frequent and more pronounced in the foam sclerotherapy treated population. Thromboprophylaxis was suggested in risk *patients. (Tables III and IV)* 

Table I. Treatment success of therapy of the great saphenous vein						
Time	6 months	l year	2 years	3 years	4 years	5 years
Surgery	97%	95%	90%	85%	83%	80%
Liquid sclerosant	83%	80%	77%	75%	72%	68%
Foam 1 shot	93%	91%	88%	85%	82%	79%
Foam 1-3 sessions	99%	96%	92%	88%		

Table II. Treatment success of therapy of the small saphenous vein						
Time	6 months	1 year	2 years	3 years	4 years	5 years
Surgery	85%	81%	77%	73%	68%	54%
Liquid sclerosant	85%	85%	83%	82%	80%	78%
Foam 1 shot	92%	87%	83%	80%	79%	76%
Foam 1-3 sessions	97%	95%	91%	89%		

Table III. Minor complications in sclerotherapy of varicose veins				
Complication	Foam sclerosant	Liquid sclerosant		
Matting	1%	0.25%		
Phlebitis	10%	4.17%		
Staining	4%	0.17%		
Skin necrosis	0.01%	0.03%		
Edema	1%	0.17%		

Table IV. Major complications in sclerotherapy of varicose veins				
Complication	Foam sclerosant	Liquid sclerosant		
Allergy	0.3%	0.7%		
TIA	0.2%	0%		
DVT	0.12%	0.07%		
PE	0.01%	0.03%		
Dyspnea/chest pain	0%	0%		
Infection	0.01%	0%		

## ULTRASOUND TECHNOLOGY AND PHLEBOLOGY NURSING

Chairpersons: A. FRONEK (USA), M. GEORGIEV (Italy)

## Leg Clubs: a patient-centered approach to leg ulcer management

E. T. LINDSAY (UK)

he main determinant for the development of leg ulceration in chronic venous disease is ambulatory venous hypertension, which acts through damage of the microcirculation. To improve the treatment of venous leg ulcers the authors have created "Leg Clubs" which are a new type of clinic where management is intensified. Leg Clubs offer a unique partnership between patients, nurses, and the local community, and are characterized by four features:

1. Based on the community, nonmedical environment

2. Collective treatment

3. No appointment required for the operation

4. Patients have a fully integrated "well leg" regime.

The authors concluded that only such an attitude to leg ulcer treatment can enhance patient compliance, healing rates, and patients' quality of life.

## Practical application of ultrasonography in assessing deep and superficial venous dynamics

S. X. SALLES-CUNHA (USA)

The author described the relationship between prevalence of reflux and diameters in the superficial veins of the lower extremity. They have used them as a guide for prosthetic valve implantation in the deep veins as well as in assessing the results of such treatment. Duration of reflux, maximum reverse velocity, and diameter of deep, superficial, and perforating veins were measured by means of B-mode color flow ultrasonography.

The authors stated:

a) On the basis of the amount of reflux and vein

diameter, endovascular prosthetic valves were implanted in the proximal femoral vein.

b) Perforating veins with a diameter larger than 4 mm always result in reflux.

c) Early symptoms are not associated with reflux in the saphenofemoral junction but with segmental reflux.

d) Deep vein diameters vary under conditions of vasoconstriction and vasodilatation.

### Vein stripping: is it an obsolete procedure?

S. HIRSCH (USA)

According to published data there is strong evidence to state that saphenous stripping is the best procedure to guarantee a low percentage of recurrences. The most frequent cause of recurrent varicose veins after surgery appears to be the presence of incompetent perforators. The rate of failure is higher if the long saphenous vein is conserved.

However, some authors have indicated that although long saphenous vein preservation could lead to recurrences in a small number of cases, at the same time it prevents nerve injuries and scars. By complete exposure of the common femoral vein and identification and ligation of all the tributaries and incompetent perforators, without stripping of the long saphenous vein, a recurrence rate of only 12% can be achieved. Because the closure of the greater saphenous vein, either with radiofrequency, laser, or sclerotherapy has become a more and more acceptable procedure, it appears that in most situations saphenous incompetence can be treated only by closure with low recurrence rate.

### A new vein in ultrasonic view

P. ZAMBONI, M. DE PALMA, S. CARANDINA, et al. (Italy)

The authors described a vein belonging to the saphenous compartment of the leg. They operated on 218 patients who suffered from primary varicose veins. To assess the great saphenous vein tributary and the presence of its homodynamic involvement in varicose networks Duplex scanning before the operation was performed. In 7% of patients a tri-

butary in the saphenous compartment of the medial aspect of the upper third of the leg was observed. It runs transversally in the interfascial compartment toward the lateral aspect of the leg for a length ranging 5 to 12 cm. A complete dissection must be done to avoid recurrences.

### **Compression and compliance**

C. L. MORGAN, B. B. BLONDEAU, L. L. TRETBAR (USA)

wo groups of patients over two periods of time (1994-1998 and 1998-2003) were compared regarding the medical benefits of compression therapy. The authors considered: age, sex, physical limitations, economic limitations, quality of life assessment, and miscellaneous complications. Significant improvement in compliance following

detailed instruction and education about compression therapy was observed in the period 1998-2002.

The conclusion was that the more educated the physicians the better treatment the patients received.

# Current concepts of chronic venous disease based on duplex scaning

N. LABROPOULOS (USA)

Duplex ultrasonography seems to be the "gold standard" in the diagnosis of chronic venous diseases (CVD). The main risk factors remain: age, sex, and family history.

Several studies have shown that both reflux in the superficial veins and reflux or obstruction of the deep venous system result in severe venous ulceration. One cannot ignore the role of perforators in the development of signs and symptoms of CVD and ulcerations. Perforator vein incompetence in the ulcerated area was detected in 28% of ulcers, and it was always associated with superficial and/or deep vein incompetence. The distribution and extent of reflux is associated with the severity of the disease but the strength of this association has not been determined because there are other reasons, such as disease duration, rate of progression, and lifestyle that play an important role.



Part 2



# **SURGICAL PROCEDURES**

## PHLEBECTOMY AND RELATED TECHNIQUES

Chairpersons: A. A. RAMELET (Switzerland), R. A. WEISS (USA)

# Combination of phlebectomy of side branches and foam sclerotherapy of the saphenous stem as a second stage

A. CAVEZZI (Italy)

**S**ince the year 2000 the author has used the therapeutic two-step combination of:

1) phlebectomy of varicose tributaries with flush ligation at the entry of the upper incompetent tributary with saphenous stem, followed by

2) duplex-guided foam sclerotherapy of the residual saphenous stem after 2 months, in patients with saphenous incompetence without saphenofemoral or sapehopopliteal junction reflux.

The sclerosant foam is formed using the Tessari method.

One to 2 months after phlebectomy no residual varicose veins are detected, and duplex imaging of the residual saphenous stem shows abolition of, or remarkable decrease in, reflux and nearly 30% reduction in diameter. No major complications have been noted. Short-and mid-term clinical and duplex follow-up are comparable with the authors' own results of foam sclerotherapy or the reported results of single phebectomy. Terminal valve competence and small calibers are the main predictive factors for a positive mid-term outcome.

### Modern phlebectomy techniques: 2003 update

A. A. RAMELET (Switzerland)

**S**ince modern phlebectomy was reinvented by R. Muller (Switzerland) 50 years ago, numerous improvements have been introduced.

- Diagnosis is accurate thanks to Doppler, duplex sonography, and diascopy (transillumination)

- Marking of varicose veins after clinical examination has been improved by duplex mapping and diascopy. Marking is done with a KmnO4 permanent pen, taking into account the influence of the patient's position.

- Tumescent anesthesia is better tolerated (painless, low toxicity, better dissection of the veins, compression effect with less bleeding and so less hematoma, rinsing effect with less hematoma, postoperative analgesic effect)

- Evolution of incision techniques, now using

needles instead of blades

- Evolution of hooks, different hooks allowing a better grasp through tiny incisions

- Absorbent bandages and selective compression decrease postoperative complications and allow immediate walking

- Evolution of the indications to more difficult veins such as: difficult areas (dilated eyelid veins), pudendal veins, dorsal venous network of the foot, reticular veins, curettage of teleangiectases, preoperative sclerotherapy, etc.

In conclusion, phlebectomy, according to Muller, has reached perfect maturity. It is a simple, elegant, and economical technique. It is easy to perform in trained hands.

# 1320 nm endovenous laser with a 280 μ fiber: equivalent to phlebectomy?

R. A. WEISS (USA)

A pilot study was performed in which nine patients with primary branches originating from incompetent greater saphenous veins were treated with a two-step approach: endovenous ablation of the incompetent greater saphenous vein (radiofrequency or laser) followed immediately by treatment of primary truncal branches with laser instead of phlebectomy. Tumescent local anaesthesia was accomplished. Due to tortuosity of the vessels, several punctures were sometimes needed to treat a segment. Direct visual confirmation of coagulation with shrinkage of vessel and lumen obliteration

was done by duplex scanning. Immediate followup (day 1 and 7) revealed no pain and no hematoma, with a fibrotic cord along the path of the treated vein. No pigmentation typical of sclerotherapy was visualized. Rupture of smaller veins does not occur with this type of laser (water heating causes thermal wall damage instead of blood absorption) More patients are needed to confirm these preliminary findings.

### Thromboembolism risk in liposuction

C. GARDE (France)

Liposuction is a safe and very common procedure. The major complication is due to embolism caused by vascular injuries. Subfascial located veins such as the short saphenous vein are not at risk. The anterior saphenous vein and Giacomini veins are at risk because they are very weak and have horizontal tributaries with the great saphenous vein. Perforator veins are linked like strings between two fixed points and are thus also at risk. There is no damage to the reticular network.

To avoid vascular injuries, preoperative mapping of important veins in the liposuction region is helpful.

A modification of coagulation in cases of trombophilia is always a specific risk increased by the crush syndrome of vascular and capillary injuries. Thus, thrombosis prophylaxis in patients with a high risk profile is mandatory. Recent venous and lower-limb surgery is a contraindication for liposuction.

The liposuction volume has to be kept below 3 liters. Operation time should not be longer than 2.5 hours. Appropriate compression therapy (lipopanty) avoids postoperative stasis.

## PHLEBECTOMY AND SURGICAL TECHNIQUES

Chairpersons: C. GARDE (France), J. A. OLIVENCIA (USA)

### Varicose surgery: regional anesthesia, elastic compression, and early walking are effective means to prevent deep venous thrombosis

M. LEFEBVRE-VILARDEBO (France)

he author presented a study of 3675 patients with 5471 consecutive venous procedures (great saphenous vein 46.2%, short saphenous vein 10.1%, inguinal or popliteal reoperation for recurrences 9.1%, atypical operations related to anatomy 30.6%) in a standard routine way to prevent DVT.

Characteristics of this routine procedure:

- preoperative skin mapping
- truncal nerve anaesthesia

- soft surgery: exclusively invagination stripping, ablation of tributaries through microincisions

- immediate 40 mm Hg elastic hosiery compression

- walking 2 to 3 hours after operation

- perioperative anticoagulation related to the medical background

All patients were clinically reviewed on day 6 to 8 and day 30. A duplex scan was performed in case of the slightest suspicion of DVT and not systematically in all patients. A thrombosis occurred in 14 patients (0.26%) with one minor pulmonary embolism. In comparison with other studies, this operative routine could be helpful in preventing DVT.

# Tumescent local anesthesia in phlebectomy: pharmacology and infiltration technique

J. A. KLEIN (USA)

he aim of this study was to find a reasonable maximum safe dose of lidocaine for tumescent local anesthesia in phlebectomy, based on our knowledge about tumescent local anesthesia in liposuctions.

Women having liposuction of the hips and thighs volunteered to participate in a 3-part study of lidocaine absorption kinetics. The author assumed a linear relationship between dosage and peak serum concentrations and concluded that an optimal dose was 40 mg/kg.

Infiltration technique with Monty needles (16 to 20 G) was proposed, in combination with the HK infiltration pump (HK Surgical). Open drainage might reduce postoperative swelling, pain, and ecchymosis.

# A novel application of tumescent anesthesia for saphenous vein stripping

L. L. TRETBAR, C. E. STUCKEY (USA)

n more than 100 cases of greater saphenous vein stripping and 15 lesser saphenous vein stripping, a new application of tumescent anesthesia was used. After local anesthesia in the groin or popliteal fossa, the stripper is brought into the vein and a tiny plastic tube is attached to the stripping bulb. Anestheticum is infused while stripping and is continued in the saphenous path after stripping.

The objectives of this study were: prolonged analgesic effect, irrigation of the stripping pathway of blood and debris, decrease in postoperative bleeding and decrease in postoperative pain. The authors concluded that there is:

- minimal blood loss (15-35 mL)
- no epinephric side effects
- prolonged pain relief
- improved ambulation the day of surgery
- decreased bruising, and swelling.

The combination of anti-inflammatory drugs and tumescent anesthesia has improved the postoperative recovery of patients with saphenous vein stripping.

# Transillumination-guided endovenous laser treatment of saphenous, perforating, and peripheral varicose veins

L. CORCOS, O. MARANGONI, L. LONGO, E. FERLAINO, D. DE ANNA (Italy)

There is a tendency towards new techniques. A modern venous procedure should be safe (no ascending thrombus), effective (no symptoms of recurrence), extensive (all varices), tolerable (no pain), rapid (short intervention time), cosmetic, cheap (instruments, material), and stable (no recurrence). A personal experience with 30 cases was described. Transillumination-guided endovenous laser treatment was combined with transillumination-guided

interruption of the junctions (minimal inguinal incision, average 10.2 mm), phlebectomy, and perforator ligation when necessary.

Complications were mentioned (residual varices 8.3%) and also the results of duplex scanning at 30 days. The technique, compared with other methods, seems to represent a safe, stable, quick, effective, well tolerated, cheap, and recommendable procedure.

# Eradication of great saphenous vein reflux also eliminates medial calf and ankle perforator vein reflux

S. J. SIMONIAN, R. R. HOLT (USA)

Ten percent of reflux in the greater saphenous vein leads to reflux in the middle calf veins and ankle perforators. It is anatomically important to know that the perforating veins connect the posterior arch vein tributary of the greater saphenous vein to the deep posterior tibial vein.

One hundred and ten lower limbs with reflux in the greater saphenous vein and perforators were operated on. A duplex scan was performed before operation, at 3 months and 1 year after operation. Eradication of the greater saphenous vein corrects perforator reflux in 85% of the cases, and this effect was still detectable after 1 year.

Reflux of the greater saphenous vein results in an increase in blood volume and secondary higher pressure in all the venous compartments. After surgery blood volume decreases and perforator reflux normalizes.

These findings suggest that perforator surgery is only indicated in a few patients.

### Three-and-four year outcomes following treatment of saphenous vein reflux using endovenous radiofrequency ablation

R. F. MERCHANT (USA)

he Closure Treatment Registry follows the outcome of limbs treated wih controlled-temperature endovenous radiofrequency ablation of the saphenous vein at annual intervals to assess the hemodynamic status of any residual vein stumps and the clinical status of the affected limbs.

In this study 318 limbs (criteria: reflux of saphenous vein, vein diameter 2-12 mm, no abnormal tortuosity or aneurysm formation) were treated with radiofrequency ablation without adjunctive high ligation and in combination with other procedures such as phlebectomy, sclerotherapy, and ligation of perforants.

Complications of the therapy were mentioned:

- paraesthesia: 1.4% (observed less frequently

when ablation was limited to saphenous vein segments above the calf)

- burns at one week: 4.2%
- DVT: 1%
- clinical phlebitis.

Absence of reflux was observed in 88% of limbs at 2 and 3 years. No evidence of neovascularization was seen. The proportion of limb pain, fatigue, and edema was low and comparable to the results of classical vein stripping. There was high patient satisfaction.

The clinical and hemodynamic outcomes of endovenous radiofrequency ablation after 3 to 4 years are encouraging and appear to be comparable to vein stripping.
### **SURGICAL PROCEDURES**

Chairpersons: L. CORCOS (Italy), P. GLOVICZKI (USA), B. B. LEE (Korea) Speakers: Z. G. WANG (China), L. CORCOS (Italy),
B. B. LEE (Korea), M. PERRIN (France), T. YAMAKI (Japan),
M. MALOUF (Australia)

Various aspects of the surgical treatment of venous and lymphatic disease were discussed during this session.

Z.G. Wang presented 14 patients investigated and treated for the Nutcracker syndrome. Reimplantation of the superior mesenteric artery below the left renal vein and transluminal angioplasty with stent deployment of the left renal vein was performed in six cases. Good clinical results were obtained. Hematuria and proteinuria after strenuous physical exercise disappeared.

L. Corcos reported various reconstructive interventions on the deep venous system in 60 patients with CVI (CEAP 3-5). He used intersection (32 cases), reconstruction by valvular transplantations (28 cases), and intravenous valvuloplasty (8 cases). Seven new reconstructive operations were performed. Damaged valves were recreated from the autologous intimal flap. All patients received class II elastic compression and 60 days of drug therapy with heparin, warfarin, and defibrotide. New reconstructive techniques led to 100% clinical improvement, 85.7% hemodynamic improvement, and 100% stable ulcer healing. The mean follow-up time was 4 years and 5 months. The author concluded that valvular repair of deep veins represents a realistic possibility.

B. B. Lee presented his experience of treating arteriovenous malformations (AVM) and chronic lymphedema. He used sclerotherapy with absolute ethanol (99 cases of AVM), embolosclerotherapy with subsequent surgical excision (16 cases of extratruncular forms AVM), and a surgical intervention in nine patients with truncular forms of AVM. Complex decongestive physiotherapy and/or sequential intermittent pneumatic compression were used for treatment of chronic lymphedema. Progression of the disease in spite of intensive treatment was an indication for surgical intervention. Such procedures as venolymphatic anastomoses, free lymph node transplantation, and resection operation were the available option.

M. Perrin has presented 72 patients (76 limbs) with isolated primary short saphenous vein (SSV) insufficiency. All these patients were treated between September 1997 and May 1978 in two skilled vascular units. Patients were grouped according to the CEAP classification and assessed postoperatively at 1 and 6 months, and later every year. Non-postoperative complications were identified in a mean follow-up period of 48 months (12 to 60 months). One recurrence in the popliteal fossa was found and treated with redo surgery 9 months after initial operation. All patients showed decreased signs of CVI (*Table I*).

Table I. Clinical result assessed by CEAP				
CEAP Class	Preop: number of limbs	Postop: (last examination) number of limbs		
C0	/	24		
C1	/	47		
C2	52	3		
C3	14	/		
C4	7	1		
C5	2	1		
C6	1	/		
Total	76	76		

M. Perrin concluded that surgical treatment of the SSV performed in specialized units gives excellent long-term results.

T. Yamaki presented an original technique of angioscopic greater saphenous vein (GSV) valvuloplasty combined with axial transposition of a competent tributary vein. This operation was performed in 59 patients with GSV incompetence. The author assessed the results of intervention with APG. Perfect results were achieved in most cases during the 36 months of follow-up.

M. Malouf described the principal causes and signs of pelvic venous congestion syndrome and presented

various methods for abolition of the ovarian vein reflux. These included the now almost obsolete retroperitoneal ligation and excision or laparoscopic ligation the more popular endovenous obliteration with coils and other occlusive materials, and also endovenous obliteration in combination with sclerotherapy.

### LIVE SATELLITE TRANSMISSION FROM SURGERY SUITES

Panel of experts: Comoderators P. RAYMOND-MARTIMBEAU (USA) and N. SADICK (USA). Produced by N. MORRISON (USA). Panelists R. ADRIAN (USA), J. J. BERGAN (USA), A. CAVEZZI (Italy), T. DAUPLAISE (USA), D. M. DUFFY (USA), A. A. RAMELET (Switzerland), P. COLERIDGE SMITH (UK), L. TESSARI (Italy), S. E. ZIMMET (USA), J. ZYGMUNT JR, (USA), R. J. MIN (USA)

his live satellite transmission from surgery suites included various methods for treating varicose veins and telangiectatic leg veins. The techniques were performed by A. Fronek, R. A. Weiss, and M. P. Goldman. Several key points were addressed. For the reticular and telangiectatic leg veins they proposed the use of a pharmaceutical solution prepared with glycerin plus epinephrine and lydocaine; this sclerosing agent has good viscosity for distribution inside the telangiectasia. They also propose the use of 1064 nm laser in the treatment of reticular veins between 0.3 and 0.7 mm.

In sclerosing treatment for saphenous collaterals, they propose the use of Sotradecol (STD) foams in 1% to 2% concentrations. In these cases they always perform echoguided injections in order to avoid extravasations.

In the treatment of great or lesser saphenous veins trunks with sclerotherapy, they propose increasing the concentrations of STD to 3%. All these injections must be performed under duplex guidance for the control of the filling of the vein up to the junction with the deep system. In order to avoid deep vein complications, several manouvers such as probe compression at the junction, extremity elevation, and leg muscular contractions after the injection are recommended.

With this protocol up to 30% of cases need to be reinjected, as Dr. Weiss pointed out.

Several cases were treated with the use of venous closure devices (1320 EVLT, 810 EVLT, VNUS Radio frequency Closure). Prior to applying any of these methods of treatment, duplex mapping of the saphenous anatomy is the single most important step, as was pointed by Dr Min. During the procedure, in order to avoid vasoconstriction of the saphenous veins, a warm temperature at the level of the venous access is mandatory.

The experts have recommended vein cannulation with the devices previous to the injection of the tumescent anesthesia. The echo image artefacts that the anesthetic liquid creates can induce problems with the correct positioning of the device at the saphenofemoral junction.

Prof J. J. Bergan has pointed out that with these techniques the classical surgical approach to the saphenofemoral junction in varicose veins disease is only necessary in cases with venous aneurysm exceeding 2 cm in diameter at the level of the preterminal valve in the junction.

Due to the high collagen properties of the venous tissue obtained after a phlebectomy, Dr Goldman proposes its use for esthetic treatment of facial wrinkles.



Part 3



### THROMBOEMBOLISM

#### **THROMBOEMBOLISM**

Moderators: BO EKLÖF (Sweden), SHUNICHI HOSHINO (Japan)

### Safety and effectiveness of combined regional thrombolysis and thrombectomy in acute lower-limb thrombosis

W. BLÄTTLER (Switzerland)

The gold standard for treatment of deep vein thrombosis is unknown. Conservative management of heparin therapy shows postthrombotic syndrome in 49.1% after 24 months.<sup>1</sup>

Heparin and compression therapy was able to reduce the frequency of postthrombotic sequelae to 20%.<sup>2</sup> Systemic thrombolysis gives a high rate of patent, recanalized vessels, but has a higher bleeding rate. Thrombectomy removes the thrombus but leads to valve damage and has an unacceptably high mortality rate. In this report, regional thrombolysis was achieved by infusing Urokinase into a dorsal foot vein after previously excluding the extremity from the circulation by a thigh cuff inflated to 300 mm Hg. The proximal veins were cleared by surgical thrombectomy with a Fogarty catheter through an inguinal venotomy. After clamping the external iliac artery, the thigh block was opened, and the thrombi flushed out by the reactive hyperemia. Blood was retrieved, washed, and retransfused. Twenty-one patients with a mean age of 25 years were treated and the maximum follow up time was 8 years in 14 patients. All patients had proximal venous thrombosis with 17 extending to the iliac region. Complications were found in 33% and 5 patients (23.8%) were reoperated on due to hematomas. There were no PE found. After 1 year 16 out of 20 patients had complete restitution, 2 had symptoms of venous claudication, and 2 showed signs of PTS. After 8 years 13/14 patients were free of PTS (93%).

In conclusion one can say that in this selected group of young patients this combined approach seems feasible, restoring vein valve function in a high number of patients.

Prandoni P et al. *Pathophysiol Haemost Thromb.* 2002;
 132(suppl 2)Abst.036.
 Brandjes DP et al. *Lancet.* 1997;349:759-762.

## Exclusion of deep vein thrombosis by measuring spot skin temperatures using a hand-held thermocomparitor

S. ENOCH (UK)

he author presented preliminary results on a novel screening tool for DVT. This instrument works on the basis of thermography but is small and portable, and could therefore be used in primary care institutions. Thirty-three patients with suspected DVT were investigated by this method and duplex scanning. The 10 patients with actual

DVT were correctly identified, and the rate of false positive results was 50%.

This new tool seems to have a high sensitivity, but a low specificity in detecting DVT, the same as thermography. Larger studies comparing it with other screening tools such as D-dimer tests will be performed.

# Incidence of deep vein thrombosis after varicose vein surgery

A. M. VAN RIJ (New Zealand)

Varicose vein surgery is often considered to be minor surgery with little risk of postoperative DVT. This is a prospective trial in 377 consecutive patients addressing this question.

Duplex scanning was performed preoperatively and 2 and 4 weeks postoperatively, and at 6 months, 1, and 3 years. The decision to give LMWH prophylaxis was left to the operating doctors. In most cases this was one or two doses of LMWH. The mean age of patients was 53 years (21 to 83 years). DVT was detected in 20 cases (5.3%), 2.1 were symptomatic. Ninety percent of DVT were restricted to calf veins; 10% were found in the popliteal vein. A positive family history for DVT, age and stage of CVI were positive predictors for DVT. There was no difference in outcome if LMWH prophylaxis was given.

In conclusion it was stated that the incidence of DVT was relatively low. LMWH prophylaxis is not suggested in patients <40 years. In at-risk patients prophylaxis should be given, but a longer period of treatment should be considered.



Part 4



### **NEWS IN RESEARCH**

#### **NEW TOPICS IN PHLEBOLOGY RESEARCH**

Chairpersons: J. MAURIELLO (USA) and E. RABE (Germany)

# Microvenous valves in the normal human lower limb and chronic venous insufficiency (CVI)

A. M. VAN RIJ (New Zealand)

Contrary to previous belief, venous valves are present not only in the macrocirculation but in microcirculation of normal limbs, and in patients with CVI. Using electron scanning microscopy, microvenous valves were observed in veins down to 20 µm in diameter in the superficial venous system. The regional distribution of valves and the size of veins containing valves were not significantly different in the normal and in venous ulcerated limbs. The concentration of the valves was greater in the proximal parts of calf than in distal parts. Differences were observed in the total density

of valves for the same compartment in both groups - patients with ulcerated limbs had a greater concentration of valves and vessels than the control group (153.8 versus 15.1 vessels / cm3, P<0.01). The ratio of vein diameter to valve sinus depth in patients with CVI was significantly greater than in normal (0.85 versus 0.61, P<0.001). In the patients with CVI, retrograde flow in microveins was observed similar to that in the macrocirculation. This is now recognized as another factor, leading to pathological skin changes.

#### Management of recalcitrant venous leg ulcers

J. D. D. VUERSTEAK (Netherlands)

**R**ecalcitrant ulcers still present a great therapeutic problem. The author presented 5 years' results of healing recalcitrant venous ulcers using a subatmospheric pressure treatment called vacuum assisted closure (VAC). Twenty four patients with venous ulcer were treated. Patients were divided into two groups – treated conventionally and with the VAC method. Compared with conventional

wound care techniques a reduction in the total healing time was seen in VAC-treated ulcers of up to 21.6%. The authors of this presentation believe that the VAC technique will become an important treatment within dermatology, not only for chronic and recalcitrant venous leg ulcers but also for arteriosclerotic and combined inoperable veno-arterial leg ulcers.

## Local endothelial function and leg symptoms in patients after deep vein thrombosis

D. N. KOLBACH (Netherlands)

n the authors' opinion, venous hypertension could lead to endothelial dysfunction, which might be expressed in local abnormalities of coagulation and fibrinolysis. They studied 15 patients with ultrasound-documented DVT in stages C-0 to C-4 of the CEAP classification. All subjects underwent ambulatory venous pressure measurements. Blood

was collected from the distal part of legs and arms after 10 minutes' standing. In patients with DVT there was a significant increase in fibrinogen and von Willebrand factor concentrations in samples from the legs. In the authors' opinion this indicates local endothelial dysfunction, which may lead to disturbances in coagulation.

#### Venous reflux measurement: (a) variability of a standardized Valsalva maneuver and venous reflux measurement (b) comparision of a standardized Valsalva maneuver and compression method

C. JEANNERET (Switzerland)

The author made a comparison between standardized Valsalva maneuver and the pneumatic compression method described by van Bemmelen. In this study 110 vein segments of 55 patients (25 M/30 F, median age 50.6 y, 24.7-71.9) with deep venous insufficiency in varicose vein disease were investigated. The standardized Valsalva maneuver (forceful expiration in the tube system, expiratory pressure of 30 mm Hg within 0.05 s held at least a 3 s) and the standardized compression method (80 mm Hg pressure distal to the investigated vein segment, held for 3 s, pressure released within 0.3sec) were performed. The common femoral vein (CFV) and the superficial femoral vein (SFV) were investigated with duplex sonography (ATL HDI 3000). Venous reflux time (RT), peak velocity (PV), and

volume flow (VF) were measured with patients standing. The correlation coefficient for the RT, PV, and VF amounted to 0.71, 0.42, and 0.6 in the CFV; and to 0.63, 079, and 0.65 in SFV. No agreement was found 14 times in the CFV (Valsalva method more sensitive P = 0.002) and 7 times in SFV. The author concluded that Valsalva and the compression method correlate best for reflux time and flow volume in the CFV and the SFV, but the Valsalva method is more sensitive in detecting venous reflux in the CFV. In this presentation were shown individual changes for parameters of venous reflux in the same compartments in following days, independent of the method of measurement used.

#### Is there duplex ultrasound evidence of neovascularization of the saphenofemoral junction following endovenous catheter ablation (EVCA) techniques - 3 years later?

N. MORRISON (USA)

**N**eovascularization has been found to be a major contributor to recurrent lower extremity superficial reflux following crossectomy with or without stripping. An alternative to stripping is endovenous catheter ablation (EVCA) which has been shown to successfully obliterate the great saphenous vein and preserve the superficial epigastric vein. The author hypothesized that EVCA used in conjunction with ultrasound-guided sclerotherapy will not

result in neovascularization and may prove to be a more effective choice in the treatment of reflux of the greater saphenous vein. In a group of 25 patients treated with EVCA and sclerotherapy there was not any revascularization observed after 3 years' follow-up. In conclusion the author suggested that EVCA with ultrasound-guided sclerotherapy may be a good alternative for replacing vein stripping.

### Gene expression profiles in varicose veins using cDNA microarray

S. J. LEE (Korea)

With cDNA microrray technology we can determine the differential mRNA expression profiles of a huge number of genes, between normal and pathologic specimens. Four patients with varicose veins and normal veins were analyzed. Among upregulated genes in the varicose veins, fibronec-

tin, versican, osteonectin, transforming growth factor, gelsolin, and connective tissue growth factor showed more than twofold increased activity. Although these findings give us insight into changes at the molecular level, these are probably secondary rather than primary factors.

### DIAGNOSTIC TECHNIQUES AND NEW RESEARCH

Chairpersons: R. J. MIN (USA) & U. SCHULTZ-EHRENBURG (Germany)

## Prognostic value of dynamic venous function tests with respect to postoperative hemodynamic outcome

M. JUENGER (Germany)

As Professor Juenger points out, it is interesting to know the exact characteristics of venous problems and to predict the results of a specific surgical treatment in our daily practice. He presented a group of 30 patients (CEAP C2-6) who were studied before and after the practice of a crossectomy plus a saphenous vein stripping in order to test whether dynamic venous function tests could predict postoperative outcome. The venous reflux and the refilling time of the leg were measured using five different methods: phlebodynamometry, three

types of photoplethysmography, and dynamic strain gauge plethysmography. Preoperatively the surgical procedure was simulated with tourniquets. The authors found a strong linear relationship between the preoperative simulated results and the postoperative situation with phlebodynamometry, strain gauge plethysmography, light reflection rheography, and light reflection plethysmography. These facts led to the conclusion that the improvement achieved with surgery can be predicted preoperatively by any one of the above tests.

# Experience with the CEAP classification in a large epidemiologic study-the Bonn vein study

E. RABE (Germany)

The German Society of Phlebology initiated an epidemiological study to evaluate the prevalence and risk factors of chronic venous diseases in the general population. From October 2000 to March 2002, 3072 members of the general population of the city of Bonn and two rural zones (age 18 to 79 years, 1350 men,1722 women) were selected via simple randomization from population registries.

They answered a questionnaire, and were examined by clinical means and duplex ultrasound. The CEAP classification was used, showing a distribution as follows C0 9.6%, C1 59%, C2 14.3%, C4 2.9%, C5 0.6%, and C6 0.1%. Pitting edema (C3) was present in 13.4%. As a conclusion, the use of the CEAP classification in epidemiological studies must be improved.

#### **Obesity and severity of venous insufficiency**

A. M. VAN RIJ (New Zealand)

The correlation between obesity and venous disorders is not clear. Theoretically obese people have a higher intrabdominal pressure that may decrease venous return and increase venous reflux. Defining as obese people with a body mass index (BMI) higher than 30, the author performed an evaluation of the venous refilling time and muscular pump function, finding a shorter refilling time and better muscle pump function when

compared with general population. By studying a varicose vein population, he found a larger size superficial femoral vein diameter, a higher venous pressure and a higher percentage of venous ulcers in obese people. This was particularly true in women. As a conclusion, he indicated that obesity worsened varicose veins, but more studies are needed to confirm these findings.

# Pathophysiologic assessments of primary varicose veins with duplex scanning

M. SAKATA (Japan)

This Japanese team presented their extensive experience in studying varicose vein population by means of duplex scan. Duplex scanning was used to examine 1606 limbs with primary varicose veins. Seventy-five percent of them (1205 limbs) had reflux at the saphenofemoraljunction (SFJ), 13% (205 limbs) at the saphenopopliteal junction, and 10% (166) in both. Incompetent perforating

veins (IPVs) were detected in 1981 limbs, mainly in the SFJ reflux group. The majority of them were direct IPVs as are Dodd, Boyd, Cockett, and paratibial IPV. They were also able to observe a correlation between the prevalence of deep venous reflux and IPVs, especially in the patients in stages C4-6.

# Quantification of hemodynamic improvement with compression stockings, using duplex sonography

B. KAHLE (Germany)

he interest of the authors in measuring femoral volume flow in vein (VFV) and artery (VFA) and the observation of greater values in the varicose vein population has led them to the description of the VAF index which is the ratio of VFV to VFA. They observed values less than 1.00 in the healthy population and superior to 1.4 in the varicose vein population. There was an improvement of these values after surgery. In this study they investigated the effect of compression therapy on the VAF

index. They analyzed the results of a group of people before and after (2 hours and 2 weeks) wearing knee- and thigh-length stockings compared with another group wearing no stockings. They observed an improvement in VAF index after compression therapy. These results led them to conclude that the VAF index is a promising tool to measure and quantify the effects of compression therapy.

### UPDATE ON FUNDAMENTAL CAUSES AND MANAGEMENT OF CHRONIC VENOUS INSUFFICIENCY

Chairpersons: J. J. BERGAN (USA), C. ALLEGRA (Italy) Speakers: P. COLERIDGE-SMITH (UK), A. JAWIEN (Poland), A. NICOLAIDES (Cyprus), M. A. PISTORIUS (France), P. SANSILVESTRI-MOREL (France)

During this symposium, some aspects of causation of chronic venous insufficiency (CVI) and their possible treatment were presented.

In discussing **epidemiology**, Prof Jawien has collected data on problems of venous disorders in the literature and has compared these with results of a recent multicenter cross-sectional study in Poland. There a prevalence of varicose veins, and severe CVI was found to be similar to that in surrounding developed countries. Risk factors including age, family history of varicose veins, obesity, and lack of physical activity were associated with chronic CVI in women more than in men.

There are few studies which have proven the importance of the **hereditary factor** at a clinical level. In an original study by Dr Pistorius to identify one or several mutations predisposing to varicose vein disease, two families have been identified and examined. This has led to determining the complete genotype of each individual within a family in order to identify new loci of interest. A potential locus has been identified, and further research is focusing on the sequencing of potential genes as well as analysis of new, large families.

Further investigations to study CVI have sought to verify whether the modified collagen composition observed in varicose veins can be reproduced in in vitro cultures. The hypothesis is that **CVI may be a systemic disease**. In fact, the abnormal collagen accumulation observed in cultures of smooth muscle and dermal cells suggests that indeed, varicose veins could be a systemic disease with a genetic etiology.

It is accepted that abnormalities in the microcirculation contribute heavily to the etiology of varicose veins as well as the chronic skin changes of CVI. Work on animal models has shown that micronized purified flavonoid fractions modulate leukocyte adhesion and prevent endothelial damage. These observations may explain the effect of such flavonoids on management of edema and other symptoms of venous insufficiency. Several studies have demonstrated that from the earliest stages of CVI, MPFF relieves symptoms of pain, paresthesia, and restless legs as well as edema. It decreases bradykinin-induced micro-vascular leakage and inhibits leukocyte activation, trapping, and migration. Now, it has been concluded that this is a first-line treatment for edema as well as other symptoms of CVI. It continues to be effective in all subsequent stages of the disease, including leg ulceration.

In summary this symposium provided an introduction to some of the most promising fields of venous research.

#### **NEW TOPICS IN ETIOLOGY AND EPIDEMIOLOGY**

Chairpersons: J. J. BERGAN (USA), E. O. BRIZZIO (Argentina), P. COLERIDGE SMITH (UK)

# Influence of pregnancy and hormones on venous diseases - results from the Bonn vein study

E. RABE (Germany)

he data from the Bonn study, a cross-sectional study conducted with the support of the German Ministry of Health, are the results of the first epidemiological study conducted in Germany after the Tubingen study of 1979.

More than 3000 people, selected via random sampling, were interviewed using a standardized questionnaire concerning general health and phlebological issues, and were examined clinically and with duplex scanning.

According to the CEAP classification, patients without any venous disease (C0) constituted 9.6%, C1 patients 59.1%, C2 14.3%, C3 13.4%, C4 2.9%, C5 0.6%, and finally C6 0.1%.

The incidence of venous disease was similar in the two sexes, and only in the C2 - C3 classes was there increased prevalence in females.

General risk analysis showed that being overweight is a risk factor for developing chronic venous insufficiency, but not for the presence of varicose veins, and that a lower social class correlates with the presence of chronic venous insufficiency. The participants were questioned on the number of pregnancies and hormone use, both as oral contraceptives and as hormone replacement therapy. Logistic regression has shown that there is a relationship between the number of pregnancies and the risk of varicose veins.

The odds ratio changes from 1.5 for women with one or two pregnancies, to 1.9 for three, to 2.1 for four, up to an odds ratio of 2.8 for females with 5 or more pregnancies.

While the risk for telangectasias, reticular veins, and varicose veins increases with the number of pregnancies, this effect is less severe for chronic venous insufficiency.

On the contrary, even if the data are less powerful, the use of hormones showed a slight reduction in the incidence of chronic venous insufficiency(CVI) with an odds ratio of 0.4.

It remains to be determined if there is any difference in lowering the risk of CVI between oral contraceptives and hormone replacement therapy.

# The incidence of venous disease in Brazil based on the CEAP classification - an epidemiological study

A. SCUDERI (Brazil)

Dr Scuderi reported on the occurrence of venous disease in the region around Sao Paulo, one of the most relevant figures from Brazil.

More than 2100 people attending the University Hospital, excluding patients from the vascular diseases departments, were given a questionnaire and clinical examination, and classified using the CEAP method.

In the male group 66.48% were 0A/0A, that is, without symptoms and without varicose veins, and similar numbers were present in the female group but only in the younger subgroup.

Subjects aged 14 to 22 years, had 46.42% at stage 0A/0A, while considering women 23 to 48 years of age, two - thirds of whom had undergone one or

more pregnancy, only 10.43% were at stage 0A/0A.

In the oldest group, 49 years and over, less than 5% were free of visible varicose veins and without symptoms, while 62.79% had both varicosities and symptoms.

This study confirms the utility of using the CEAP classification, and shows results similar to those obtained in epidemiological studies in Western countries; venous diseases appear more common in females than in man, age and number of pregnancies are correlated with the presence of the disease, and up to 50% of young women may have altered veins, without symptoms, but suffer aesthetic discomfort.

#### A meta-analysis of venous leg ulcer healing in prospective randomized studies using micronized purified flavonoid fraction

P. GLOVICZKI (USA)

A meta-analysis to evaluate the efficacy of micronized purified flavonoid fraction (MPFF, Daflon 500 mg, Servier, France) in addition to conventional treatment for the healing of venous leg ulcers was presented.

In his introduction, P. Gloviczki reminded that more than 1% of adults will suffer from leg ulcers at some time and that the costs associated with the long-term care of these chronic wounds are substantial. In a recent survey performed in the US,<sup>1</sup> the number of new patients has been evaluated to 20 556 each year. Twelve per cent of ulcer patients usually require hospitalization. Annual direct costs has been estimated to USD 150 million to 1 billion. These did not included indirect costs (loss of work days, early retirement, reduced quality of life).

Compression therapy remains the cornerstone of management in venous leg ulcer provided the material used (usually, several layers of elastic bandage), 30 to 40 mm Hg, is able to provide sustained pressures, and is correctly applied. Despite these recommendations, not all ulcers are healed. Thus, the question of the benefit of a systemic pharmacotherapy as an adjuvant to standard compression therapy has been studied. MPFF was chosen for its well - known protective effect on the microcirculation. MPFF indeed appears to work by decreasing the interaction between leukocyte and endothelial cells, reducing the capillary increased permeability. It acts by inhibiting expression of endothelial intercellular adhesion molecule-1 (ICAM 1), and vascular cell adhesion molecule (VCAM), as well as surface expression of some leukocyte adhesion molecules (monocyte or neutrophil CD 62 L, CD11B).

The objective of this meta-analysis was to assess the ability of MPFF used in combination with conventional treatment (ulcer management and compression) in improving the process of venous leg ulcer healing.

Seven comparable, prospective, randomized, controlled studies were identified from medical literature databases and from the files of the manufacturer in which 723 patients with venous ulcers were treated with MPFF (2 tablets daily) or placebo for at least 2 months (1 study) and up to 6 months (4 studies). The percentage of patients with complete healing of the reference ulcer at 6 months was taken as the primary end-point. Secondary end-points consisted of: time to healing after in clusion (in days), rate of complete healing at month 2 and month 4 (% patients completely healed), reduction of reference ulcer area (in % of healed surface), and decrease in associated symptoms

(% patients without heaviness and pain).

When compared with controls, ulcer healing at 6 months was in favor of MPFF (61.3% vs 47.7%; RR: 1.32; CI: 1.03-1.70; P=0.03). This was significant from month 2 (RR=1.44, CI=1.07-1.94; P=0.015), and associated with shorter time to healing (P=0.0034), greater reduction of ulcer area (P=0.016 and 0.005 at months 4 and 6 respectively), and greater improvement in symptoms (P<0.005 at months 2, 4, and 6).

These results, along with those of previous individual randomized, controlled trials, confirm that MPFF accelerates the process of venous leg ulcer healing.

1. Heit JA, Rooke TW, Silverstein MD, et al. Trends in the incidence of venous stasis syndrome and venous ulcer: a 25-year population-based study. *J Vasc Surg.* 2001:33;1022-1027.

#### **Constitutional functional venopathy**

C. ALLEGRA (Italy)

Starting from a clinical approach, and listening to patient complaints, the authors focalized on a group of symptoms, which in their view constitute a new clinical entity.

Out of more than 4000 patients studied annually, about a quarter presented with leg discomfort without visible varicose veins, or reflux in the superficial or deep venous system.

These patients presented with a group of symptoms which mainly include edema, heavy legs, subcutaneous fat "cellulite," acral hypothermia, menstruation irregularities, and blood pressure values at the lower limit of normal.

In addition to clinical and ultrasound methods, a subgroup of patients were also assessed with capillaroscopy, blood samples for hormonal studies, microlymphography, and laser Doppler. A significant decrease in progesterone and a significant increase in prolactin were documented, while microcirculatory investigations showed venular hypertension, microlymphatic overload, and a prepuberal capillaroscopic picture, leading to a decreased venous tone, even in the absence of reflux.

The diameter of the saphenous junction in clino and orthostatism showed an increase of 4.2 mm.

The hormonal disturbances could account for the edema, menstrual disturbances, and subcutaneous adipose tissue alterations, and the microcirculatory findings could explain the venous symptoms without venous reflux.

These patients, if correctly identified, could improve with modification of their lifestyle, and with the use of venoactive drugs.

# Prospective epidemiological study of developing varicose veins over a period of two decades (Bochum Study I-IV)

U. SCHULTZ-EHRENBURG (Germany)

The Bochum studies investigated the preclinical and early stages of venous disease, examining a group of students from secondary schools, starting at the ages of 10 to 12 years, and following a group of them up to the age of 29 to 31 years.

The subjects were examined with a questionnaire, measurements, physical exam, photoplethysmography, Doppler ultrasound, and, for the Bochum IV study, with Duplex Scanner.

The results are summarized in Table I.

Even if the decrease in the number of subjects studied, especially in the Bochum IV study, could lead to some selection bias, the study has shown that while reticular varices are present at an early age, telangectasias become apparent later and increase with age.

Varicose veins were essentially present in the

Bochum IV study, but reflux in the saphenous vein was present far ahead of visible varices. Females presented with more telangectasias and reticular varices, but tributaries and incompetent perforators were more frequent in men.

A hereditary trait was shown, with all types of varices and reflux that correlated with a positive family history.

The increase of the prevalence is - age and - growth - related.

The ultrasound detection of reflux usually precedes the clinical appearance of varicose veins, and offers opportunities for preventive measures.

Photoplethysmography did not appear suitable for early detection of venous disease.

Table I. Results of the Bochum studies (I to IV)						
RESULTS:						
	Bochum I	Bochum II	Bochum III	Bochum IV		
	(1982/83)	(1986/87)	(1990/91)	(2001/02)		
	AGE: 10-12	AGE: 14-16	AGE:18-20	AGE: 29-31		
	N = 740	N = 518	N = 459	N = 136		
<b>REFLUXES:</b>						
LSV	12.4%	10.4%	13.5%	20.6%		
SSV	0.1%	1.9%	6.3%	5.9%		
LARGE VARICES:						
LSV	0.0%	1.6%	2.0%	11.0%		
SSV	0.0%	0.2%	1.3%	1.5%		
TRIB.	0.0%	0.8%	5.0%	17.7%		
PERF.	0.0%	0.8%	5.2%	25.7%		
<b>SMALL VARICES:</b>						
RET.	10.7%	30.3%	35.3%	74.3%		
TEL.	0.0%	3.7%	12.9%	50.4%		



Part 5



### **SPECIAL TOPICS**

#### **COMPRESSION**

Chairpersons: J. CAPRINI (USA), H. PARTSCH (Austria)

# The influence of the dynamic elasticity coefficient on the action of compression therapy

H. A. M. NEUMANN (Netherlands)

n the presented paper, the author challenged the official CEN measurement technique for prediction of the dynamic effect of different compression hosiery in the same compression class. The second conclusion was that differences in hysteresis of

the hosiery can lead to differences between static and dynamic behavior of compression hosiery. Low hysteresis in the knitwear makes hosiery more effective, with greater hysteresis the hosiery is comparable to nonelastic or textile elastic bandages.

# The role of compression in preventing postthrombotic syndrome

H. PARTSCH (Austria)

Partsch studied 37 patients 2 years after DVT. Eleven had been treated by bedrest and 26 by walking with either bandages or compression stockings. There was a significant decrease in swelling measured in 10 out of 11 of patients who had been treated by bedrest, and in 15 out of 26 of

patients who were treated by compression and walking. Seven of the 11 of patients in the bedrest group suffered from pain, versus 10/26 in the walking group. In conclusion, compression and walking is an active therapy to avoid postthrombotic pain swelling.

#### Recurrent varicose veins: our experience with 5-year follow-up

C. ALLEGRA, A. CARLIZZA, M. BARTOLO (Italy)

he authors shared their experience of proceeding with recurrent varicose veins. They emphasized the role of echo and color Doppler in the diagnosis of the location and the morphology of the lesion, especially in the choice of the operative technique. Over 12 years, 1326 patients underwent surgery on varicose veins.

The patients were divided into four groups, according to the location of intervention:

- 1. Primary great saphenous vein 65%
- 2. Primary small saphenous vein 10%
- 3. Primary associations 8%
- 4. Secondary varicose veins, great saphenous vein area 17%.

Overall new recurrences at 5 years were 37.7%.

Group 1. 12.6% (A1 SF junction only - 29 patients, A2 - SF junction + Hunter canal perforators – 29 patients, A3 SF junction + Hunter canal perforators + leg perforators - 51 patients)

Group 2. 29.5% Group 3. 36% Group 4. 65%

The authors concluded that the location of the incompetent perforator vein (above or below the knee) and previous DVT play a leading role in the occurrence of recurrent varicose veins. The second conclusion is that the consequent surgical procedure could change the number of recurrences of varicose veins in groups 3 and 4.

#### A combined compression system for treatment of venous leg ulcer influence on venous hemodynamics and clinical efficacy

J. STREJCEK (Czech Republik)

he authors presented a new method of healing venous leg ulcers that they call double-step watercushion. This simple cushion made of fine, nonallergic rubber, is partially filled with water. One part of the cushion is fixed under the sole and the other in the ulcer region. During walking the water is squeezed from the peripheral part to the part placed

on the ulcer. The authors verified the activation of the muscle pump by means of duplex ultrasound and photoplethysmography.

In spite of reports in the literature about the advantage of minimally invasive methods over conservative treatment, the authors expected high clinical efficacy in healing of venous leg ulcers.

### POINT-COUNTERPOINT IN VEIN DISORDERS: AN INTERACTIVE DEBATE

Chairpersons: A. CORNU-THENARD (France), P. RAYMOND-MARTIMBEAU (USA), J.-F. UHL (FRANCE).
Panel of experts: J. P. BENIGNI (France), J. J. BERGAN (USA),
J. CAPRINI (USA), P. COLERIDGE SMITH (UK), M. FORRESTAL (USA),
A. FRULLINI (Italy), C. GARDE (France), J. L. GILLET (France),
L GRONDIN (Canada), J. J. GUEX (France), D. HILL (Canada),
M. LEFEBVRE-VILARDEBO (France), M. PERRIN (France),
A. A. RAMELET (Switzerland), M. SCHADECK (France), F. VIN (France)

n this special interactive session several clinical cases were presented and discussed by a panel of experts. The audience had the opportunity to share their experience of different clinical therapies through an electronic voting system.

In the treatment of telangiectasia and reticular veins, there was a general consensus in the use of sclerotherapy over other methods such as lasers. When treating matting, Dr Grondin proposed the use of telangiectatic ablation with multiple needle punctures.

Regarding the medical and surgical dilemmas in the treatment of large veins, different issues were raised. The increasing use of foam sclerotherapy and of several endovenous closure devices rather than classical surgical management became obvious. These less invasive therapies allow the treatment of older people, who in the past would have been treated only by means of compression. The panellists cited ongoing studies that show excellent clinical results at 3 years with the use of foam sclerotherapy in the great saphenous vein compared with surgery.

Dr Caprini emphasised the important aspects of a correct clinical, hemodynamic, and radiological assessment when dealing with patients with edema and ulcers. Among the different treatment options, only the efficacy of compression therapy has been shown with randomized trial methodology, and is now a 1A grade level recommendation with an ulcer recurrence rate of 29% to 38%.

Dr Raymond-Martimbeau emphasized the importance of syringe aspiration before each injection, a correct choice of the dosage, and concentration of the sclerosing agent, and the use of US-guided monitoring when dealing with medium to large veins in order to avoid complications such us pigmentation and skin necrosis. She presented a case of severe pigmentation that occurred 7 years earlier, and reported how the appearance improved using a liposuction aspiration tissue technique.

### **SPECIAL TOPICS SESSION #1**

Chairpersons: A. FRONEK (USA) A. NICOLAIDES (Cyprus)

#### Rollercoaster reflux: definition and clinical significance

W. S. GRADMAN (USA)

Using ultrasound methods, namely Duplex scanning, it is possible to easily identify reflux pathways that typically descend from a leaking point to a varicose vein.

At the same time, it is possible to identify subjects in whom the reflux originates at a lower point, ascends 10 or even 20 centimetres, and then descends again, with a pattern that has been described by previous authors as paradoxical flow, but that can be graphically described as a "rollercoaster reflux."

Duplex scanning is able to identify the exact origin of the reflux, and direct digital compression is able to abolish the filling of the varicose vein.

In 11 patients with this kind of reflux, the source of reflux was the femoral vein in three cases, the popliteal vein in two, the great saphenous in three, the small saphenous in two, and the tibial veins in one case.

The affected veins were the great saphenous in three cases, the Giacomini vein in two cases, and in six cases collateral veins were involved.

Being able to recognize this kind of reflux makes it possible to correct it surgically, with good clinical results.

# Factor XIII-mediated inhibition of fibrinolysis accelerates healing of venous leg ulcers

Y. HEROUY (Germany)

Factor XIII has been used topically to treat venous leg ulcers using the rationale that ulcers have a high fibrinolytic activity, and that subjects with factor XIII deficiency have difficulties in healing wounds.

Twenty patients were examined with Duplex to confirm the diagnosis, and 10 were treated with Factor XIII, while 10 received a placebo treatment. All the patients received conventional compression therapy.

The ulcer area was assessed using a computerized system that allows measurement the ulcer area expressed as number of pixels.

The subjects had punch biopsy before and after the topical treatment.

The fibrinolytic activity was increased in the placebo group and had no variation with treatment, while the patients that received topical Factor XIII showed a significant decrease. At the same time, ulcer healing was accelerated, and the ulcer area was decreased after the first week of treatment.

The author suggests that Factor XIII is an effective antifibrinolytic drug that used topically can accelerate venous leg ulcer healing.

#### Elastic compression stockings in the prevention of the post-thrombotic syndrome after deep vein thrombosis: a meta-analysis

D. N. KOLBACH (Netherlands)

Compression therapy is traditionally used in treating patients with deep vein thrombosis, but the evidence that this treatment reduces the occurrence of post-thrombotic syndrome has rarely been assessed.

The authors did a search of Medline, EMBASE, Cochrane controlled trials register, and used hand searching and personal communications, to look for confirmed deep vein thrombosis and nonpharmaceutical interventions.

Three randomized controlled trials were identified, two of them comparing elastic stockings with a compression of 30 to 40 mm Hg at the ankle against no intervention, after deep vein thrombosis, while the third study used stockings with 20 to 30 mm Hg compression, and stockings one or two size larger, as placebo.

In the treatment group only 32% developed postthrombotic syndrome, compared with 62% in the control group, with an odds ratio of 0.32, while considering only severe post-thrombotic syndrome the odds ratio was 0.39, favoring treatment. No serious side effects were mentioned.

There is evidence enough to suggest that elastic compression stockings should be systematically added to the treatment of deep vein thrombosis, to

prevent post-thrombotic syndrome.

It remains unclear when to prescribe the stockings, for how long, and what the effect is of different compression classes.

## Changes of venous valvular function in patients with chronic venous disease undergoing heat stress

T. OGAWA (Japan)

The authors studied 25 subjects with chronic venous disease, using a Duplex scanner to measure vein diameter, peak reflux velocity, reflux time and volume, after 5 minutes in a cold bath at 15° and then after 5 minutes in a bath at 40°.

The common and superficial femoral veins were studied, together with the great saphenous vein.

Eight refluxes appeared after the hot bath, two in

the superficial system, and six in the deep veins, and vein diameter increased in all cases. The authors conclude that heat stress deteriorates venous function.

This observation could have practical applications considering that patients are studied at different times of the year, and under different temperature conditions.

#### Corona phlebectatica: clinical and hemodynamic significance

J. F. UHL (France)

Corona phlebectatica, also called malleolar or ankle flare, is defined as fan-shaped intradermal telangectases on the medial or lateral aspect of the foot.

In the CEAP classification, it is part of the C1 class definition, but there is controversy on the importance of this finding as a prognostic tool.

Using classification software, called CVR, the authors studied 347 patients, and found that ankle flare was present in 27.5%, and it was graded as

severe in 13, moderate in 25, and mild in 54. It seems to be correlated with the severity of the disease, and particularly with reflux in the perforators, but it appears to occur early.

Its prognostic significance is unclear.

Longitudinal studies will be required in order to validate it as a valuable tool for the clinical prediction of the development of severe chronic venous disease.

# Efficacy of a short-stretch tubular compression orthosis compared with a short-stretch bandage in the treatment of venous leg ulcers

M. JUENGER (Germany)

he treatment of venous leg ulcers is based on local compression.

It is usually accomplished using short-stretch bandages, that have the disadvantage of tending to slip and lose shape; above all their efficacy is highly dependent on the skill of the fitter.

Using a new short-stretch tubular compression orthosis, Tubulcus, that exerts a 30 to 40 mm Hg pressure at the ankle level, appropriate pressure is applied, independently the skill of the fitter.

One hundred and eighty-eight patients suffering from ulcers not older than 3 months with a maxi-

mum diameter of 5 cm were studied in 32 centers for 12 weeks. Half were treated with the new orthosis, and half with a short stretch bandage applied by experienced personnel.

The study showed that there was no significant difference between the two groups, and that a commercial compression device can compare favorably with an expertly applied elastic bandage.

The side effects mainly consisted of discomfort, and a choice of size well-suited to the patient is indispensable.

#### The effects of elastic stockings on venous hemodynamics

M. M. FIGUEIREDO (Brazil)

While compression stockings are an evidencebased therapy for chronic venous disease, it is not so easy to quantify the effects they exert.

The use of an air plethysmograph allowed the author to study 29 limbs of 17 patients, in CEAP classes 4 and 5, before, during, and immediately after wearing compression stockings.

The venous reflux was reduced with the stockings, as expressed by a reduction in venous filling index,

and the venous volume was reduced too, but the calf muscle pump function was only slightly affected, and the ejection fraction and residual volume fraction were virtually unaffected.

As soon as the stocking is removed, the beneficial effects are no longer exerted, and the plethysmographic parameters return to their initial value.

#### Placebo compression stockings: myth or reality?

H. PARTSCH (Austria)

n assessing the efficacy of compression stockings, some studies use stockings one or two size larger, as placebo.

These stockings are supposed to be devoid of active properties, but using special equipment to measure the pressure under the stockings, it was found that stockings two sizes too large, as compared with almost 35 mm Hg exerted by fitting II class stockings, exert a pressure of slightly more than 5 mm Hg. Studying 20 volunteers with venous occlusion magnetic field plethysmography it was found that a very mild (5 mm Hg) pressure is able to increase venous outflow (nonsignificant), to reduce swelling (nonsignificant), and to increase tissue compliance (P > 0.001).

So some effects can be expected, as long as the stockings do not slip down, and real placebo compression does not exist.

### **SPECIAL TOPICS SESSION #2**

Chairpersons: N. MORISSON (USA), H.A.M. NEUMANN (Netherlands)

#### **CEAP** revised classification

A. CORNU-THENARD (France)

The current C covers all the aspects of the classification, and moreover the external consistency is good, so why create a new classification?

After the UIP in Rome, other definitions and refinements were suggested.

C 4, skin changes, covers pigmentation, eczema, lipodermatosclerosis, atrophie blanche, and as lipodermatosclerosis and atrophie blanche are more closely related to the pre-existence of an ulcer, C4 a and C4 b were created.

The same pathway was followed for corona phlebectatica, known from the Widmer Classification. Corona is a sign of chronic venous insufficiency over a long period and the prevalence of corona is related to edema, so C3 a and C3 b were created.

We need a computerized venous registry to evaluate the need for a new classification.

Table I. Suggested changes in the CEAP classification					
Current C	Proposed C				
<b>C0</b> no visible or palpable signs	<b>C0</b> no visible or palpable signs				
Cl teleangiectasies	<ul><li>Cl a teleangiectasies</li><li>Cl b reticular veins</li></ul>				
C2 varicose veins	<ul><li>C2 a varicose veins</li><li>C2 b recurrent varicose veins</li></ul>				
C3 edema	<ul><li>C3 a edema</li><li>C3 b corona phlebectatica</li></ul>				
C4 skin changes	<ul><li>C4 a pigmentation-eczema</li><li>C4 b lipodermatosclerosis-atrophie blanche</li></ul>				
<b>C5</b> skin with healed ulcer					
<b>C6</b> skin with active ulcer					

#### Changes in endothelial activity caused by venoactive drugs measured by photoplethysmography and circulating endothelial cells

J. STREJCEK (Czech Republic)

mpairment of endothelial activity is one of the early signs of vascular disease development. Changes in endothelial activity are also present in chronic venous insufficiency. These changes can be detected by several methods. In this paper photoplethysmography and counting of circulating endothelial cells in veins was used.

It is presumed that a venoactive drug stabilizes the endothelial cells in the veins and causes an increase in their activity.

In a group of 37 patients with chronic venous insufficiency (CEAP 3-4) the authors measured:

- number of circulating endothelial cells
- number of circulating endothelial cells after venous stress (leg occlusion)
- changes in endothelial activity after acetylcholine iontophoresis

After 2 months of venoactive drug (troxerutinum 300 mg, heptaminol 300 mg, extract of ginkgobiloba, twice a day) the results were compared with those obtained before treatment and in a group of untreated volunteers in CEAP 3-4.:

- increase in endothelial stability as a statistically significant lower number of
- circulating endothelial cells after 2 months of treatment
- increase in endothelial activity measured by photoplethysmography after acetylcholine iontophoresis

These results demonstrate, by two independent methods, an increase in endothelial stability after 2 months of medication with a combination of venoactive drugs.

# Primary sclerotherapy registry and trial; the sclero 10-year, randomized CVI study

G. BELCARO (Italy)

This study compared two sclerosing agents, sodium tretradecyl sulfate and athoxy-sclerol. A comparable group of patients aged 25 to 65 with uncomplicated chronic venous insufficiency and varicose veins were included.

Patients were divided into three groups according to the vein diameters, and the concentration of

sclerosing agent and duration of compression was indicated.

Three-month and 6-month vein closure, skin reactions, systemic reactions, local inflammation, pain, target vein trombosis, tolerability, and main trunk 5-and 10-year closure were investigated. They were all significantly in favour of A ethoxy-sclerol.

Group A	diameter >3 mm	concentration 3%	compression 3 weeks
Group B	diameter 2.9-1.1 mm	concentration 1-2%	compression 1-3 weeks
Group C	diameter < 1 mm	concentration 0.5%	compression < week

#### Ultrasound features of sciatic nerve varices

S. RICCI (Italy)

**S**ciatic nerve varices are believed to be a rare clinical finding. Patients present with a symptomatology of sciatic pain because the vein follows the fibular saphenous nerve, its mother branch, the common fibular nerve at the popliteal site and the great sciatic nerve in the thigh.

On clinical examination one sees typical small or large varicose veins on the anteroposterior part of the leg (appearing just below the popliteal crease and extending lateral to the small saphenous vein), and a painful point can be found at the site of the "vein disappearance" below the popliteal crease. Clinical diagnosis must be confirmed by color duplex: this shows a superficial varicose vein lateral to the small saphenous vein, becoming subfascial at the popliteal crease for a short distance and progressively getting deeper in the thigh muscular spaces. The vein described follows the fibular saphenous nerve.

One patient was treated with foam sclerotherapy, with a good clinical result at 1-month follow-up examination.

Another patient was treated the same way by another specialist, and this resulted in an irreversible nervus fibularis palsy.

# Efficiency in the treatment of perforating veins in combination of transilluminated miniphlebectomy and preoperative duplex ultrasound

A. FLOR (Austria)

here are different modalities of treatment for insufficient perforant veins in cases of severe chronic venous insufficiency. SEPS requires increased technical requirements which are costly, and phlebectomy is sometimes inappropriate because one cannot determine the exact localization where the vein perforates the fascia. A cheap and effective method has been proposed by the author.

He starts with a preoperative mapping of the perforating veins by duplex ultrasound.

Peroperatively, a luminiferous 5-mm rod which features at its oblique tip a cannular opening to

allow the flow of saline or tumescent solution is inserted into the subcutaneous tissue. After hydrodissection, the xenon light emerging from the rod provides excellent visualization of the suprafascial perforating veins. The perforating veins are then retrieved by means of the hook through microincisions above the place of fascial perforation.

In this way, unnecessary manipulation and the total amount of stich incisions can be reduced in a diseased skin region.

# Popliteal vein entrapment as a cause of multiple recurrences of small saphenous vein insufficiency

R. MILLERET (France)

The study included 8 patients with recurrences of small saphenous vein insufficiency who had been operated on twice or more.

**Symptomatology**: leg pain when standing and walking, swelling of the leg in the early morning, tension of the calf.

**Clinical findings**: unequal in calf diameter, swelling of the calf during exercise, rarely disappearance of posterior tibial artery pulse during plantar flexion.

**Diagnosis**: duplex scanning, confirmed by dynamic ascending phlebography which shows compression of the deep veins at the popliteal level during active plantar flexion of the foot.

**Treatment**: surgery is only performed in cases of positive dynamic phlebography. Under general anesthesia, the popliteal fossa is explored through an incision after M. Perrin (longitudinal incision of the skin, vertical incision of the fascia). The popliteal vein is dissected free with section of any fibrous element that mighty compress the vessel. After removal of the varicose recurrences, the vena poplitea is closed with a Teflon patch.

**Results**: No complications occurred and the patients were relieved of symptoms, calf diameter decreased, and there was no recurrence after a mean period of 18 months.

### **SPECIAL TOPICS SESSION #4**

Chairpersons: A. FRONEK (USA), M. SCHADECK (France)

# Venous hemodynamic mapping (VHM): terminology and symbolism

S. MANDOLESI (Italy)

Concepts and terminology related to venous hemodynamic surgery have been in constant evolution since its initial description in 1988. There are several institutions worldwide performing this type of surgery for the treatment of varicose veins, and the authors presented the most recent and widely accepted terminology used in this surgical strategy. The main purpose of this classification is to divide the veins of the lower extremities into four systems:

1. R1: all the veins inside the deep fascia

2. R2: all the veins between the superficial and deep fascia (greater and lesser saphenous veins, Giacomini and anterior saphenous vein)

3. R3: all the veins in the subcutaneous tissue

4. R4: those veins in the R3 system connecting two R2.

With this type of division different types of venovenous shunts between these systems are described, and a surgical strategy can be developed and drawn in a diagram (*Figure 1*).

In our view this is a very practical way of approaching varicose disease with an echoguided surgical strategy, directed to the identification of the refluxing points, and the elimination of shunts. Further worldwide consensus and discussion on this matter is important, as well as future results of several prospective studies that are under way.



Figure 1. Division of veins of the lower extremities.

#### Venous hypertension, inflammation, and valve remodeling

M. N. PASCARELLA, (USA)

Blood flow is directly related to the pressure in blood vessels, as was demonstrated by Poisseuille in 1884. Different blood flow patterns (laminar vs turbulence), change the shear stress which in turn regulates physiological vascular responses. Turbulent flow has been found to be capable of triggering an inflammatory reaction through leukocyte activation and transmigration into the vascular wall.<sup>1</sup> The authors presented very interesting work, with the objectives of defining the key elements of venous inflammation in its early stages, and also defining the anti-inflammatory effects of micronized purified flavonoid fraction (MPFF) (Daflon 500 mg, Servier, France). For this purpose they created a model of venous hypertension in mice performing an AV fistula in the right groin, with ligation of the epigastric vein and the femoral vein above the fistula (Figure 1).



Figure 1. Femoral artery and vein, ard adjacent anatomy.

The study design included 35 animals separated in these groups:

STUDY GROUPS	ANIMALS
Controls, contralateral vein	5
A-V shunt, untreated	15
A-V shunt, MPFF (50 mg/kg/d)	8
A-V shunt, MPFF (100 mg /kg/d)	7

The authors studied the leukocyte infiltration (*Figure 2*), adhesion molecule expression (*Figure 3*), apoptotic markers, transcription factors, and preformed intravital microscopy of gracilis muscle microcirculation.



attenuated by MPFF in a dose-dependent manner



Several interesting conclusions are obtained from this new model of venous hypertension:

1. In this model of leukocyte infiltration, adhesion molecule expression and apoptosis of endothelial cells, the hallmarks of inflammation, are seen.

2. Veins subjected to AV fistula pressure show

lesions mimicking the findings in human surgical specimens

3. MPFF attenuates the inflammatory process in a dose-dependent manner.

#### **References:**

1. Takase S, Lerond L, Bergan JJ, Schmid-Schönbein GW. *Am J Physiol Heart Circ Physiol*. 2002;282:HI387-HI394.

### Combined endovenous laser and duplex-guided foam sclerotherapy in the treatment of varicose veins

M. N. ISAACS (USA)

With the objective of reducing the incidence of varicose veins collaterals that can be present after treatments of greater or lesser saphenous veins trunks with laser therapy, the authors proposed a method of combined laser and duplex-guided foam sclerotherapy of open distal segments and abnormal open branches with foam sclerosing agents.

The proposed method starts with the usual procedure for endovenous laser. After placement of the laser catheter in his place, the vein distal to catheter insertion is treated with foam 3% STD, 2 to 4 cc in total, while deep vein junction is compressed. After perivenous tumescent anesthesia is administered, endovenous laser is performed as usual.

The authors presented a group of 84 veins treated without combined foam sclerotherapy and a rate of 18% persistent open segments and a short series of 17 veins in patients with the combined therapy and a 6% rate of persistent open segments.

Although the number of patients in the combined therapy group is somewhat low to draw a conclusion, from duplex-guided foam sclerotherapy complements endovenous laser in a safe way, resulting in fewer open segments requiring further treatments.

# Current laser and light-based technology in the treatment of leg veins

R. ADRIAN (USA)

he purpose of this study was to improve the understanding of the mechanism of action of different lasers are employed in the superficial treatment of small varicosities.

The response to laser therapy is often seen histologically as a decrease in vessel size, intravascular coagulation, endothelial damage, and an increase in perivascular collagen (*Figure 1*).

Although recent advances in our understanding of pulse duration and pulse delivery have increased safety and efficacy, most practitioners are disappointed with the lack of consistent clinical improvement achievable with all these systems. Pulse dye lasers are associated with significant dermal hemorrhage, but the main problem with these systems remains the postprocedural long-term hyperpigmentation.

The speaker concluded that in his wide experience with lasers, sclerotherapy is by far the best way to treat leg vein varicosities.



Figure 1. Laser-induced changes in dermal tissue.
# Telangiectases and reticular veins: how to quantify treatment results

J. F. UHL (France)

The presence of telangiectases is often an indicator of a complex incompetent venous network beneath the skin. The recent use of transillumination has been a first step in realizing some reticular mappings. The authors presented a new system (VARITAS), based on a computerized digital imaging technology that allows a record of the precise location of the reticular and telangiectatic veins

and to compare and validate the results of different treatments (*Figure 1*).

Pixel-counting quantitates the degree of abnormality of each lesion. A comparison of the pixel count before and after treatment quantitates efficacy of treatment and allows statistical analysis. The system is still under development and not commercially available



Figure 1. Computerized mapping of pre-and posttelangiectasia treatment.

## **CVI AND ULCERATION**

Chairpersons: J. CHUNGA CHUNGA (Peru), A. J. COMEROTA (USA)

#### Skin manifestations of CVI

A. A.RAMELET (Switzerland)

The author presented a review of all the main skin disorders resulting from CVI. He divided them into two groups:

a) acute manifestations: purpura, contact and stasis dermatitis, infections, panniculitis, drugrelated eruptions, and necrosis

b) chronic manifestations: "dermite ocre," teleangiectasias, pseudo-Kaposi (acroangiodermatitis), dermatitis, lymphedema, papillomatosis, liodermatosclerosis, calcifications, atrophie blanche, and leg ulcers.

It is important to realize that venous hypertension

may also aggravate all types of dermatoses of the leg, such as psoriasis or lichen rubber planus on one hand, and can induce hyperhidrosis or diminution of follicular features on the other. In the short discussion that followed, some of the audience suggested that CVI can lead to many types of skin inflammatory disorders. The conclusion of the presentation was that CVI includes numerous skin manifestations, and it would be an advantage for specialists in phlebology also have experience in dermatology.

#### Incompetent perforating veins of the foot

I. UCHINO (USA)

his short presentation discussed incompetent perforating veins of the foot. Similarly to other areas, valvular insufficiency was considered to be present when venous reflux was over 0.5 seconds. About 90% of these veins are localized in four anatomical regions of the foot: near the lateral and medial malleolus and the lateral and medial sole of midfoot.

Localized varicose veins, clusters of spider veins, skin pigmentation, and ulcers are the typical signs of these disorders.

Investigation was performed in a small group of patients with typical signs of perforating veins insufficiency of this area using continuous wave Doppler ultrasound and color-flow duplex imaging. The results were very interesting:

- 88% of incompetent perforating veins were found in typical anatomical regions
- All incompetent veins were diagnosed by continuous wave Doppler ultrasound
- Color flow duplex Doppler documented incompetent perforating veins only in 50% of the time
- Over 90% of incompetent perforating veins were associated with venous reflux of the leg.

In conclusion, the author suggests that venous reflux of the leg may be a possible etiologic factor which leads to perforating vein insufficiency in the foot region.

#### Venous leg ulcers and apoptosis: a TIMP 3-mediated pathway?

Y. HEROUY (Germany)

he causes of vein pathology are still unrecognized. A new method of investigation – molecular biology – may provide answers to questions on many important subjects such as apoptosis. There are several genes in human DNA which are recognized as inducers of programmed cell death. However, not only genes regulate programmed cell death. There are many intra-and extracellular factor, that can initiate this process. One of them is the tissue inhibitor of metalloproteinase -3 (TIMP-3). The prodeath domain of TIMP-3 resides in its N-terminal region, and apoptosis is induced by the activation

of a signaling cascade involving caspase-8 and caspase-9.

The results of these investigations provide evidence that venous leg ulcer could be the result of an apoptotic signaling pathway which may be induced through a TIMP-3 mediated inhibition of proteinase-dependent extracellular matrix degradation. These results suggest that controlling programmed cell death may have therapeutic potential in preventing venous ulceration.



Part 6



## **AVF SYMPOSIUM**

## AMERICAN VENOUS FORUM SYMPOSIUM. THE MANAGEMENT OF VENOUS DISORDERS: GUIDELINES OF THE AMERICAN VENOUS FORUM

Chairpersons: P. GLOVICZKI (USA) A. J. COMEROTA (USA)

# **Current management of acute iliofemoral venous thrombosis:** the AVF guidelines

A. J. COMEROTA (USA)

What is the goal of therapy of deep vein thrombosis? We want to prevent the worst immediate consequences, such as pulmonary embolism, but in the long term we must also prevent the postthrombotic syndrome, a highly debilitating situation that frequently results from iliofemoral venous thrombosis, especially if both venous incompetence and venous obstruction are present.

There are studies showing that an aggressive approach to eliminate clots via a surgical approach or local thrombolysis can lead to good patency results and improve quality of life. One large, randomized, national multicenter trial, called TOLEDO, has just been approved by the Food and Drug Administration.

Considering the current options available, the author suggests that for acute iliofemoral deep vein thrombosis, catheter-directed thrombolysis is the option of choice, using thrombectomy in patients where thrombolysis is contraindicated, correcting any eventual stenosis of the venous system, and subsequently putting the treated patients on anticoagulant therapy.

# The CEAP Classification: update based on recent Pacific and Caribbean consensus meetings

B. EKLOF (Sweden)

The CEAP classification is 10 years old, having arisen from discussions during the fifth annual meeting of the American Venous forum, in 1993, where the idea of using a system similar to that of the TNM classification for cancer was launched.

The next national meeting saw the creation of an international ad hoc committee, chaired by Professor Nicolaides, that produced a consensus document.

CEAP stands for a classification of chronic venous disease that is based on Clinical manifestations, Etiologic factors, Anatomy, and Pathophysiologic findings.

The document enjoyed a very wide distribution, and was published worldwide in dozen of journals, in at least eight languages. Important contributions were made at a Paris meeting in 1998, and during an international consensus meeting organized in Rome in 2001.

In 2002 the President of the American Venous Forum appointed an ad hoc committee to review the classification and present the results of their work in 2004.

The actual prospective is to maintain the overall structure of the CEAP classification, adding precise definitions of its four components.

The results are eagerly awaited, as the CEAP classification has shown its worth in getting researchers to speak the same language worldwide, and allowing the daily practice to achieve a scientific analysis of treatment alternatives.

#### Current guidelines for evaluation of chronic venous disease

F. T. PADBERG, Jr (USA)

he clinical score of the CEAP classification has been complemented by severity scoring systems, elaborated by an American Venous Forum committee on venous outcomes.

On the Venous Clinical Severity Score (VCSS) 10 clinical characteristics of chronic venous disease are scored from 0 for their absence, up to 3 for a severe manifestation.

The Venous Disability Score (VDS) divides the patients into four grades, from a symptomatic (score 0) to unable to perform their daily activities, even wearing compression (score 3).

The Venous Segmental Disease Score (VSDS) grades major venous segments according to the presence of reflux and obstruction.

These scores appear to be clinically useful, and have been tested for reliability.

Other useful data for characterizing chronic venous disease can arise from the patients themselves, and are the various Quality Of Life questionnaires, which complement the information obtained by doctors, from the patient's point of view.

Other aspects that must be assessed are the results of ultrasound and physiological studies.

Much remains to be done in specific areas such as "why doesn't this ulcer heal?," the influence of morbid obesity, calf pump dysfunction, and more subtle aspects of chronic venous disease.

# Current guidelines for management of symptomatic venous reflux and varicose veins

E. J. HARRIS, Jr (USA)

Superficial venous insufficiency usually requires correction of great saphenous vein reflux. The gold standard intervention for the management of great saphenous vein reflux remains high

ligation and stripping of the vein to the knee. It has been shown that ligation and stripping give better results than ligation alone.

Up to now, no benefits have been proven for sclerotherapy when compared with stripping of larger vessels.

Today preoperative Duplex ultrasound is an important adjunct to our clinical studies.

Ultrasound-guided foam sclerotherapy is a new technique that is widely used, and could prove to be more effective than the traditional methods.

Endovascular saphenous ablation is a new and successful technique that uses radiofrequency resistive heating along the vein wall to obtain closure of the vein itself.

Thermal skin injury appears to be the main adverse effect in 2% to 3% of the patients.

A similar technique is laser obliteration, which, from preliminary reports, appears to have good results, similar to radiofrequency ablation, with lower costs and decreased treatment times.

Further studies will demonstrate whether the initial results of these techniques can be maintained in the long term; up to now we can say that the recurrence rate favours stripping.

The main advantage of these new techniques consists in the patient losing fewer working days compared with venous stripping, and it is one of the main reasons why such procedures can show an advantage in costs over conventional interventions. Moreover the patient's satisfaction after surgery is higher after these innovative methods, even if there is no difference after 4 months of therapy.

We still need long-term objective follow-up studies to properly address the role that each single procedure will have in the future.

# Guidelines for nonoperative treatment of advanced chronic venous insufficiency and local treatment of venous ulcers

P. COLERIDGE SMITH (UK)

Compression treatment is effective in the management of varicose veins, preventing edema and helping to obtain up to 70% ulcer healing, even if the bad news is that with venous leg ulcers we have a 25% annual recurrence.

Using drugs to treat ulcers make sense, as the underlying cause for ulceration does not appear to be reflux alone, there being little difference in the reflux patterns of subjects with chronic venous insufficiency with or without ulceration.

Many drugs have been applied topically, but none of them have been shown to have great effect, and some can harm the patient, sensitizing the skin around the ulceration.

Only two drugs have been successfully tested in patients with venous leg ulcers.

Pentoxiphilline is one of them, and eight randomized controlled trials have confirmed a benefit in ulcer healing using this drug, with six patients needing to be treated to achieve one healed ulcer.

Flavonoids, namely micronized purified flavonoid fraction, have quite recently been the subject of a meta - analysis that has collected original data from five prospective, randomized, controlled, multicenter studies.

This meta - analysis has demonstrated that adding micronized purified flavonoid fraction to conventional compression therapy gives a significant advantage in ulcer healing time, and that there is also a significant reduction in ulcer area compared with conventional therapy.

Moreover, there is also a significant improvement in patient symptoms.

They should be used as an adjunct to the conventional therapy based on compression and surgical correction when possible, but it has been shown that drug therapy is an effective and cost-saving adjunct to conventional treatment.

# Current guidelines for surgical, endoscopic, and endovenous treatment of advanced chronic venous insufficiency

P. GLOVICZKI (USA)

Chronic venous insufficiency is a widespread disease, and when advanced to the point of causing leg ulceration, it has a huge social and economic cost.

When the main cause appears to be superficial vein incompetence, surgical intervention appears to be the most rational approach.

However, even in fully compliant patients, the recurrence rate is not negligible.

A treatment of incompetent perforators can be suggested in these cases, and this can be accomplished in several ways, namely by conventional surgery, but there is still room for subfascial endoscopic perforator surgery (SEPS), a technique that uses an endoscopic approach.

Its benefit has not been clearly demonstrated, but in an institution such as the Mayo clinic, about 12% of perforator surgery is approached through the SEPS technique.

In treating large-vein obstruction, with high pressure gradients, the placing of stents has proved useful.

Treatment of incompetent perforators can be useful, and we need more studies to compare the SEPS technique with more conventional interventions and determine its place in venous surgery.



Part 7



## **UIP INITIATIVES AND AWARDS**

## **UIP INITIATIVES AND AWARDS**

Chairpersons: C. ALLEGRA (Italy), H. PARTCH (Austria)

#### The "C" of CEAP: suggested definitions and refinements. An International Union of Phlebology Conference of Experts

A. CORNU-THENARD (France)

The CEAP classification was created in order to facilitate meaningful communication about CVD and serve as a basis for a more scientific analysis of management alternatives. It was found that intraobserver reproducibility was 85% while interobserver was of 47%. A conference of experts on its refinement met at the 14th World Congress of the International Union of Phlebology in Rome (September 2001).

The key points they worked on were the definitions of clinical items and the refinements of the "C" of CEAP. They considered 3 mm to be size limit of a reticular vein, because this discriminates better between class 1 and class 2 than 4 mm.

They have taken into account "corona phlebectatica," but it is still not clear where to locate this in the CEAP.

The last refinement refers to C4 (skin changes) making a differentiation between C4a, such as eczema and pigmentation, and C4b, such as lipodermatosclerosis and atrophie blanche.

#### Tightening tight junctions with compression therapy

Y. HEROUY (Germany)

Transcellular (channels and carriers) and paracellular (tight junctions) pathways are responsible for water and solution exchanges.

The tight junctions are localized on the apical side of endothelial cells (zona occludens) and are the major regulators of permeability. Tight junctions are created by several molecules (occludin, claudin 1, 3, and 5) which influence the passage of fluids. The aim of this study was to determine if these junctions are involved in the pathology of chronic venous insufficiency.

The mRNA and protein expression pattern of tight junction molecules was studied in 8 patients with edema, 8 patients with venous leg ulcers, and 8 healthy control subjects.

Biopsy specimens were taken before and 4 weeks after compression therapy. mRNA-expression was determined by using reverse-transcriptase and polymerase chain reaction and protein-expression by Western blot from tissue specimens.

Quantification performed to determine the expression

for tight junction molecules displayed diminished expression of claudin-1 and -5 in patients with chronic venous insufficiency in comparison with healthy controls on mRNA as well as the protein level. No statistical differences could be detected for occludin and claudin-3 between the edema group and the healthy group. There was a significantly elevated expression of mRNA and protein level for occludin and claudin-3 in the leg ulcer group in comparison with the healthy group.

After 4 weeks of compression therapy there was significantly elevated expression of claudin -1 and -5 on mRNA and protein level than prior to treatment for both the edema and the leg ulcer group. Occludin and claudin-3 levels did not change. So, compression therapy tightens the paracellular pathway via elevated expression of specific tight junction molecules, and thereby prevents the progression of chronic venous insufficiency due to inhibited permeability of fluid into the perivascular tissue.

#### Nomenclature of the veins of the lower limbs: an International Interdisciplinary Consensus Statement

A. CAGGIATI, (Italy)

he anatomy of the veins of the lower limbs is extremely variable. Associated with this fact there is a deficiency in the nomenclature of these veins that is leading to confusion and a misinterpretation of the appropriate methods in the treatment of venous disease.

In September 2001, during the 14th World Congress in Rome and under the auspices of the IUP, a consensus document regarding the nomenclature of the veins of the lower limbs was developed, with some important changes in the terminology.

The veins of the lower extremities are divided into three systems: the superficial, the deep, and the perforating venous systems. These are located in two main compartments: the deep compartment (bounded by the muscular fascia), and the superficial compartment (bounded deeply by the muscular fascia and superficially by the dermis).

Within the superficial compartment a separate saphenous compartment must be introduced. This compartment is bounded superficially by the hyperechogenic saphenous fascia. (*Figure 1*)

The names of a few deep veins have been changed and the list has been extended. The term "superficial femoral vein" should not be used because it is a deep vein, so only the "femoral vein" designates the vein that originates from the popliteal vein and courses the femoral canal. The term "sural veins" is not sufficient to designate the venous system in the calf. This should be designated as "soleal veins" and "gastrocnemius medial and lateral veins."

In the superficial compartment the names of some veins have also been changed. The term "great saphenous vein" (GSV), should be used instead of terms such as long saphenous or internal saphenous vein. In the same way the term "small saphenous vein" (SSV), should replace the previous short, external, or lesser saphenous vein.

The perforating veins have been associated frequently with personal names from a historical point of view. Instead these veins are classified on the basis of their topography and divided into: perforators of the gluteal muscles, perforators of the thigh, perforators of the leg, ankle perforators, and perforators of the foot.

This new terminology which was published in the *Journal of Vascular Surgery*, in August 2002,<sup>(1)</sup> will facilitate the appropriate international exchange of information.

#### **References:**

1. Caggiati A, Bergan J.J., Gloviczki P, et al. Nomenclature of the veins of the lower limbs: An international interdisciplinary consensus statement. *J Vasc Surg.* 2002;36:416-422.

Figure 1. Compartments (superficial and deep) of the venous system in lower extrimities.



#### The role of the programmed cell death (apoptosis) regulatory mechanism and the level of apoptic gene expression as a factor responsible for the occurrence of primary varicose veins

T. URBANEK (Poland)

Apoptosis is involved in many vascular diseases. Until now there have been very few data available concerning the role of PCD (programme cell death) in chronic venous insufficiency. In the presented paper an importance of the apoptosis, its stimulus factors and regulatory mechanisms (p53, p21, bax, bcl-2, and Fas) in patients with primary varicose veins were investigated. According to the morphometric analysis of the vein wall content (collagen, elastin, SMC-smooth muscle cells) in patients with varicose veins, a significant accumulation of the extracellular matrix was documented, with concomitant reduction of the SMCs within the vein media. This process can be related to the SMC phenotype change into secretory one. Apoptosis is a process controlling the vein wall hemostasis, leading to a decrease in the number of SMCs (pathological

cell elimination). In patients with varicose veins this process is downregulated and leads to the accumulation of the extracellular matrix (probably stimulated by TGF -  $\beta$  activity). In the paper the correlation between apoptotic index (TUNEL assay) and p53 expression (RT-QPCR) was documented in young patients with primary varicose veins. In the vein wall adventitia the presence of inflammatory cells (macrophages and lymphocytes) was confirmed, however, in patients with varicose veins lower proapoptotic protein Bax expression in this layer was observed. Apoptosis is an important factor for vein wall homeostasis maintenance, and plays an important role in the vein wall changes leading to varicose vein occurrence.

#### Elastin dysregulation in varicose veins

M. GEMMA PASCUAL GONZALEZ (Spain)

t has been established that a reduction in the level of elastin plays an important role in the appearance of varicose veins (VV). Elastin is formed of the reticulation of tropoelastin monomers over a framework of fibrillin-rich microfibrils and latent transforming growth factor- $\beta$  binding proteins (LTBPs). LTBPs modulate both the expression and the deposition of growth factors such as tissue growth factor- $\beta$  (TGF- $\beta$ ) in the extracellular matrix and thereby, is able to regulate the development of elastic tissue. Lysyl oxidase (LOX) belongs to a heterogeneous family of enzymes that oxidize primary amine substrates to reactive aldehydes. LOX

is known mainly for the extracellular catalysis of lysine-derived cross-links in fibrillar collagens and elastin.

Little is known about some venous wall compounds as fibrillin and LTBPs, and factors involved in tissue remodeling in which LOX and TGF- $\beta$  are involved. The aim of the research performed in the framework of the 2003-2005 UIP Fellowship is to examine, in vitro and in vivo, the expression of LOX, tropoelastin RNAm, and the pattern expression of different elastic fibre components found in the extracellular matrix of varicose veins.





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# SERVIER UIP RESEARCH

#### Members of the selection committee:

C. Allegra (Italy), A. Bradbury (UK), H. Caldevilla (Argentina), J.J. Guex (France), H. Partsch (Austria), A.A. Ramelet (Switzerland)

## \$30 000 grant for an international project in the field of phlebolymphology

#### 2001 winner: Dr URBANEK (Poland)

**Project:** The role of apoptosis regulatory mechanisms in the occurrence of primary varicose veins

#### ✓ 2003 winner: Dr PASCUAL GONZALEZ (Spain)

Project: Elastin dysregulation in varicose veins

Next winner awarded at the 2005 UIP World Congress in Rio de Janeiro and invited to the 2007 UIP Chapter to present the project results



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The Research Fund of the **Union Internationale de Phlébologie (UIP)** is proud to announce the fourth **Servier Research Fellowship**. It will provide a 30 000 USD grant for 2 years' work on a research project in the field of **phlebolymphology** selected through a highly competitive peer-review procedure.

The competition is open to young candidates who have a specific interest in the field of phlebolymphology and are a member of a national society in this field. The projects must consist of **original clinical or basic research** in an area of phlebolymphology, such as anatomy, physiology, pathophysiology, diagnostic methods, or clinical research. The fellowship will be made available from 1 November 2005 and end in October 2007.

The review of the submitted projects and the selection of the best candidate will be made by a committee of **recognized worldwide specialists** in the field of phlebolymphology.

Send us your project at the following address:

Jean-Jérôme GUEX Fonds de Recherche de l'UIP 32, boulevard Dubouchage 06000 Nice, France

The last research fellowship winner, Dr Maria Gemma PASCUAL GONZALEZ (Vascular Biology, Spain) was awarded the grant at the 2003 UIP Chapter in San Diego for her project "Elastin dysregulation in varicose veins."

Candidates must submit a synopsis of 8 to 10 pages, double-spaced, typewritten in English, in the form of 5 original printed copies. The synopsis should clearly present the objectives, methodology, planning, and references of the projected work. Candidates must also submit a curriculum vitae and a letter from a referee supporting the project and confirming its backup, together with details of how the fellowship money will be spent. After the first year of work, the award-winner must submit to the committee a synopsis of progress so far. The project's results will have to appear in a form suitable for publication in an international journal.

Next winner awarded at the UIP World Congress in Rio de Janeiro (October 2005)

> Invitation to the 2007 UIP Chapter to present the project's results





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