



Recommendations for the endovascular treatment of varicose veins by echo-guided injections of sclerosing foam: the Grenoble 2008 expert consensus.

For more information, or to download and sign the recommendations please log on the site: la-mousse.com

Implemented by the Foam Club (group of vascular physicians treating varices by endovascular procedures).

Presidents: Gilles GACHET – VOIRON 38 - gigal@orange.fr
Laurent SPINI – PONTDE BEAUVOISIN 38 - SPINI.LAURENT@wanadoo.fr

Pilot group: Drs Jean-Patrick BENIGNI – PARIS, François BUCCI – GRENOBLE, Jean-Marc DIAMAND – GRENOBLE, Gilles GACHET – VOIRON, Jean-Luc GILLET – BOURGOIN-JALLIEU, Jean-Pierre GOBIN – LYON, Jean-Marie GUEDES – RIOM, Jean-Michel LECOQ – RIOM, Bernard MARABELLE – CANNES, Olivier PICHOT – GRENOBLE, Laurent SPINI – PONT de BEAUVOISIN.

Reviewers: Pr Patrick-Henri CARPENTIER, Drs Karim BEN BARKA, Sophie BLAISE, Jean-Paul CAMUZET, André CORNU-THENARD, Serge COUZAN, Guy FRANCO, Didier LEBRUN, Wassim MAZLOUM, Didier RASTEL, Hervé RIOM, Yann ROUSSIN, and Charles ZARCA.

FOREWORD.

Why are recommendations needed?

For a long time, surgery was the standard treatment for saphenous varices but the recent breakthroughs in endovascular treatment and especially the development of sclerosing foam changed perspectives in phlebology considerably. This change of practice lead us to, write these recommendations, outlining the medical scientific context which still require validation by ruling authorities: HAS (Haute Autorité de Santé = Higher Health Authority), AFSSAPS (Agence Française de Sécurité Sanitaire des Produits de Santé = French Health Products Safety Agency), the University, and medical administration with the CNAM (Caisse Nationale d'Assurance Maladie = National Insurance Health Fund). Establishing a consensus also seemed necessary to have a medico-legal basis for legal and judicial instances such as the CNO (Conseil National de l'Ordre = French Medical Council), patient associations, insurance companies, etc.

These recommendations based on experience of the authors and current scientific data should be a reference for colleagues wishing to learn this method. Furthermore, it will form the basis of Assessment of Professional Practice (APP).

Methodology.

These rules for good practice were collectively drafted by a group of vascular physicians experienced in phlebology, members of the Foam Club. This consensus document was elaborated in compliance to HAS criteria (1). It was based on numerous international studies and publications demonstrating the efficiency and safety of this treatment (2- 28). It was submitted to reviewers (university professors, vascular surgeons, general practitioners, patient associations) and updated according to the evolution of the technique and results of ongoing scientific studies. It was elaborated without any external financial help. The members of the pilot group were not paid for their participation and had no financial link with industries in this field.

Glossary of abbreviations.

GSV, great saphenous vein

SSV, small saphenous vein

DVT, deep venous thrombosis

LMWH, low-molecular-weight heparin

VKA, vitamin K antagonists

CEAP, clinical, etiological, anatomic, and pathophysiological classification of venous disease

CHIVA, ambulatory conservative hemodynamic treatment of venous insufficiency

SPI, systolic pressure index or ABPI ankle brachial pressure index

MRI, magnetic resonance imaging

G, gauge

F, French.

NSAID, non-steroidal anti-inflammatory drug

History (29)

The first sclerosing injections were performed in LYON by C.G. Pravaz, in 1840. In 1939, E.R. Mac Ausland sampled the foam of shaken morrhuate sodium and injected it. This was the first foam injection. In 1946 E. Reiner sclerosed a varix with a detergent (sodium tetradecyl sulfate) for the first time. The same year, Egmont James Orbach described the air-block technique which was to separate the sclerosing fluid from venous blood with air. At the same time, Raymond Tournay elaborated the French procedure for proximal to distal treatment of reflux. After 1980, continuous wave Doppler, mode B ultrasonography, black and white and then color duplex ultrasound dramatically changed the investigation and then the treatment of venous disease with the introduction of echo-guided sclerotherapy by Vin and Knight in 1988 (30). In 1986, Grigg made foam by connecting 2 syringes to a tube (Irvine technique). In the 90s Cabrera (31), Monfreux (32), Mingo Garcia (33), Tessari (34), Gachet (35), Sadoun (36), Onorati (37), and others developed spread endovenous foam procedures. Thus, the concept and the clinical use of sclerotherapy using foam are not recent.

Mode of action and interest in foam.

Foam sclerosant is made with detergents or surfactants which will dissolve the phospholipids of the venous wall. Unlike sclerosing fluid which dilutes in blood, requiring staged injections with high concentrations, foam remains undiluted and, after displacing the blood adheres to the vein wall and induces an intense spasm. Thus it is now possible to treat the whole of a varicose system with a single injection at low concentration. Venous valves may become competent again as local hemodynamics function normalizes by suppressing both the siphon effect and venous hypertension. Some vein segments which were varicosed do not need any other treatment.

BIBLIOGRAPHY.

1. Bases méthodologiques pour l'élaboration de recommandations professionnelles par consensus formalisé. HAS janvier 2006.
2. ANAES. Traitements des varices des membres inférieurs, Juin 2004. Journal des maladies vasculaires. 2005;30;1:14-44.
3. J.P. Henriet. Foam sclerotherapy : state of the art. Editions Phlébologiques Françaises 2002.
4. Breu FX, Guggenbichler S, Wollmann J-C. 2nd European Consensus Meeting on foam sclerotherapy 2006 Tegernsee, Germany. VASA 2008;37(Suppl 71):1-30.
5. Rabe E, Pannier-Fischer F, Gerlach H, Breu F-X, Guggenbilcher S, Zabel M. Guidelines for Sclerotherapy of Varicose Veins. Dermatol Surg. 2004;30:687-693.
6. J.P. Gobin J.P, J.P. Benigni J.P. La sclérothérapie. Editions ESKA 2007.
7. Cabrera J, Cabrera J, Garcia-Olmedo M.A. Treatment of varicose long saphenous vein with sclerosant in microfoam form: long term outcomes. Phlebology. 2000;15:19-23.
8. Tessari L, Cavezzi A, Frullini A: Preliminary experience with a new sclerosing foam in the treatment of varicose veins. Dermatol Surg. 2001;27:58-60.
9. Cavezzi A. Sclérothérapie à la mousse (méthode de Tessari) : étude multicentrique. Phlébologie. 2002;55:149-53.
10. Cavezzi A, Frullini A, Ricci S, Tessari L. Treatment of varicose veins by foam sclerotherapy: two clinical series. Phlebology. 2002;17:13-8.
11. Frullini A, Cavezzi A. Sclerosing foam in the treatment of varicose veins and telangiectases: history anal safety complications. Dermatol Surg. 2002;28:11-5.
12. Hamel-Desnos C, Desnos P, Wollmann JC et al. Evaluation of the efficacy of polidocanol in form of foam compared to liquid forming sclerotherapy of the greater saphenous vein: initial results. Dermatol Surg. 2003; 29:1170-5.
13. Yamaki et al. Comparative study of duplex-guided foam sclerotherapy and duplex-guided liquid sclerotherapy for the treatment of superficial venous insufficiency. Dermatol Surg. 2004;30:718-22.
14. Barrett JM, Allen B, Ockelford A, Goldman M. Microfoam ultrasound -guided sclerotherapy of varicose veins in 100 legs. Dermatol Surg. 2004; 30:6-12.
15. Guex J.J. Foam Sclerotherapy: An Overview of Use for Primary Venous Insufficiency. Sem vascul 2004;12;008:25-28.
16. Kakkos S.K, Bountouroglou D.G, Azzam M, Kalodiki E, Daskalopoulos M, Geroulakos G. Effectiveness and Safety of Ultrasound -Guided Foam Sclerotherapy for Recurrent Varicose Veins: Immediate Results. J Endovasc Thera. 2006;13:357-364.
17. Alos J et al. Efficacy and safety of sclerotherapy using polidocanol foam: a controlled clinical trial. Eur J Vasc Endovasc Surg. 2006;31:101-7.

18. Cabrera J. Microfoam sclerotherapy. *Semin Cutan Med Surg.* 2006;24:175-83.
19. Coleridge Smith P. Chronic Venous Disease Treated by Ultrasound Guided Foam Sclerotherapy. *Eur J Vasc Endovasc Surg.* 2006;32;577-583.
20. Buselmeier TJ. Foam sclerotherapy. *Phlebology.* 2006; 21:105.
21. Darke S.G, Baker S.J.A. Ultrasound -guided foam sclerotherapy for the treatment of varicose veins. *British Journal of Surgery.* 2006;93:969-974.
22. Myers K.A, Jolley D, Clough A, Kirwan J. Outcome of Ultrasound -guided Sclerotherapy for Varicose Veins: Medium-term Results Assessed by Ultrasound Surveillance. *Eur J Vasc Endovasc Surg.* 2007;33:116-121.
23. Wright D, Gobin J.P, Bradbury A.W, and coll. Varisolve ® polidocanol microfoam compared with surgery or sclerotherapy in the management of varicose veins in the presence of trunk vein incompetence : European RCT, *Phlebology.* 2006;21,4:180-190.
24. Ceulen R.P.M, Yolande I, Bullens-Goessens J.M, Sebastien J, PI-Van De Venne A, Patty Y, Nelemans J, Joep C, Veraart J..M, Sommer A. Outcomes and Side effects of Duplex-Guided Sclerotherapy in the Treatment of Great Saphenous Veins with 1% versus 3% Polidocanol Foam: Results of a Randomized Controlled Trial with 1-Year Follow-Up. *Dermatol Surg.* 2007;33:276-281.
25. Hamel-Desnos C, Ouvry P, Benigni J-P et al. Sclérothérapie échoguidée de la grande veine saphène. Comparaison de la mousse à 1 % et 3 % de polidocanol. Résultat à 2 ans d'une étude en double aveugle randomisée. *Eur J Vasc Endovasc Surg.* 2007;34:723-729.
26. Jia X, Mowatt G, Burr J.M, Cassar K, Cook J, Fraser C. Systematic review of foam sclerotherapy for varicose veins. *Br J Surg.* 2007;94:925-36.
27. Hamel-Desnos C, Ramelet A.A, Guias B. Efficacité des mousses de sclérosants : synthèse des principaux essais cliniques publiés. *Angéiologie.* 2004 ;56,2:39-44.
28. Rabe E, Otto J, Schliephake D, Pannier F. Efficacy and safety of greater saphenous vein sclerotherapy using standardised polidocanol foam (ESAF) : a randomised controlled multicenter clinical trial. *Eur J Vasc Endovasc Surg.* 2007;nov 5.
29. Wollmann JC. The history of sclerosing foams. *Dermatol Surg.* 2004;30:694-703.
30. Knight R.M, Vin F, Zygmunt J.A. Ultrasonic guidance of injection into the superficial venous system. *Phlébologie.* 1989. A.Davy, R.Stemmer. John Libbey Eurotexte;339-341.
31. Cabrera Garido J.R, Cabrera Garcia-Olmedo J.R, Garcia-Olmedo Dominguez M.A. Elargissement des limites de la sclérothérapie : nouveaux produits sclérosants. *Phlébologie.*1997;50:181-8.
32. Monfreux A. Traitement sclérosant des troncs saphéniens et leurs collatérales de gros calibre par la méthode MUS. *Plébologie.*1997;50:351-3.

33. Mingo Garcia J. Esclerosis venosa con espuma : Foam Medical System. Revista Espanola de Medicina y Cirurgia Cosmetica.1999;7:29-31.
34. Tessari L. Nouvelle technique d'obtention de la scléro-mousse. Phlébologie. 2000 ;53:1,129.
35. Gachet G. Une nouvelle méthode simple et économique pour confectionner de la mousse pour sclérose échoguidée. Phlébologie.2001;54:357-360.
36. Sadoun S. Description de deux techniques pour fabriquer de la mousse de sclérosant. Phlébologie.2001;54:357-60.
37. Onorati D. Nouvelle méthode de production de mousse de sclérosant. Phlébologie.2002;55:369.
38. Carpentier P-H., Lacroix P, Guilmot J-L, Fiessinger J-N. Formation initiale des médecins vasculaires : une mise à jour nécessaire ! Journal des maladies vasculaires.2007;32,177-189.
39. Perrin M. Quelles compétences pour le phlébologue médical en 2010 ? Phlébologie. 2008 ;61;1,71-72.
40. Laroche J-P, Dauzat M, Coupé D-B-M, Böge G, Khauvankien A, Galanaud, J-P, Quéré I. Vers une clarification des techniques de l'écho-Doppler vasculaire : journal des maladies vasculaires. 2007; hors série:01.003-S26.
41. Rao J, Goldman M. Stability of foam in sclerotherapy : differences between Sodium Tetradecyl Sulfate and Polidocanol and the type of connector used in the double-syringe system technique. Dermatol Surg 2005;31:19-22.
42. Sadoun S. In : Gobin JP, Benigni JP, eds. La sclérothérapie. Paris: Editions Eska; 2007:65-70.
43. Barret J.M, Allen B, Ockelford A, Goldmann M.P. Microfoam ultrasound -guided sclerotherapy treatment for varicose veins in a subgroup with diameters at the junction of 10 mm or greater compared with a subgroup of less than 10 mm. Dermatol Surg. 2004;30;11:1386-1390.
44. Sica M. Traitement de varices de plus de 8 mm de diamètre par échosclérothérapie à la mousse et contention. Phlébologie. 2003;56:139-45.
45. Guex JJ. Contre-indications de la sclérothérapie. Journal des maladies vasculaires. 2005;30:144-9.
46. Regan JD, Gibson KD, Ferris B, et al. Safety of proprietary sclerosant microfoam for saphenous incompetence in patients with R-to-L shunt: interim report. J Vasc Interv Radiol 2008;19:Suppl:S35-S35.
47. Aguirre L. Le foramen ovale perméable et son implication dans les complications de la sclérothérapie à la mousse : le point de vue du cardiologue. Phlébologie.2007; 60;4,387-388.
48. Morrison N. How to improve results and reduce side effects ? Phlebologie.2008 ;37;4,211-220.

49. Tejedor C, Guex JJ. Foramen ovale perméable et sclérothérapie. *Phlébologie*.2008;61;3,319-331.
50. Donnet A. Migraine, accident cérébral et sclérothérapie à la mousse : le point de vue du neurologue. *Phlébologie*.2007; 60;4,389.
51. Gachet G, Spini L. La sclérothérapie des varices sous anticoagulants. *Phlébologie*. 2002; 55;1:41-44.
52. Coleridge Smith P, Labropoulos N, Partsch H, Myers K, Nicolaïdes A, Cavezzi A. Examen écho-Döppler des veines des membres inférieurs dans la maladie veineuse chronique. Texte de consensus de l'union internationale de phlébologie. *Phlébologie*. 2007;60;3:271-291.
53. Lance G. Barrelier MT. La sclérothérapie. In : Boissier C. Guilmot JL, éd. *Thérapeutique en médecine vasculaire*. Paris: Editions Masson; 1995:115-8.
54. Becker F. Current Treatment of Varicose Veins. *Vasc disease*. 2006; 8;2;97-103.
55. Pichot O, Sessa C, Bosson J.L. Duplex imaging analysis of the long saphenous vein reflux: basis for strategy of endovenous obliteration treatment. *International angiology*. 2002;21:333-336.
56. Gachet G. Une nouvelle stratégie pour traiter les varices à la mousse de sclérosant : le «Save Our Veins concept» ou SOV concept. *Phlébologie*. 2007;60;1:35-43.
57. Hamel-Desnos C., Desnos P. L'échosclérothérapie à la mousse en 2004. Technique de la ponction-injection directe. *Phlébologie*. 2004; 57;3;289-300.
58. Gachet G. La sclérose échoguidée par Bras porte-sonde. *Phlébologie*. 1998;51;2:221-223.
59. Cabrera J. Traitement des veines saphènes par injection avec un cathéter court de micromousse de Polidocanol sous contrôle échographique. In : Gobin JP, Benigni JP, eds. *La sclérothérapie*. Paris: Editions Eska;2007:77-89.
60. Milleret R. Sclérose des veines grandes saphène à la mousse délivrée par cathéter long échoguidé sur veine vide « Alpha-Technique » In : Gobin JP, Benigni JP, eds. *La sclérothérapie*. Paris: Editions Eska; 2007: 91-95.
61. Vin F, Bénigni J-P. Conférence internationale de consensus sur la compression. *Phlébologie*. 2003;56:315-65.
62. Gillet JL, Guex JJ, Allaert FA, Chleir F. Incidence des complications de la sclérothérapie à la mousse : résultats de l'étude de la Société française de Phlébologie. *Phlébologie*. 2005; 58:349-351.
63. Gillet JL, Guedes JM, Guex JJ, Hamel-Desnos C, Schadeck M, Lauseker M, et al. Side effects and complications of foam sclerotherapy of the great and small saphenous veins : a controlled multicentre prospective study including 1025 patients [abstract]. 9th Annual Meeting of the European Venous Forum; 2008 June 26-28; Barcelona.
64. Sellier-Franchitti D. Procédures d'urgence : une check-list au cabinet. *Phlébologie*, 2003;56;3:293-297.

65. Natali J, Poulain J.C. L'angiologue et le chirurgien vasculaire face aux juges. Editions Ellipses;1999.

66. Benhamou A.C, Natali J. les accidents des traitements sclérosants et chirurgicaux des varices des membres inférieurs. A propos de 90 cas. Phlébologie. 1981;34:41-51.

67. Marabelle B. Attitude pragmatique face au risque juridique en phlébologie. Phlébologie. 2006;59;4: 357-363.

68. Loubry N. Conformité des locaux et des moyens. EMC 50-270-D-10,2000.

1/ TRAINING.

Handling the foam is difficult and requires good knowledge of anatomy and venous diseases, experience in duplex ultrasound practice (thrombosis, reflux, cartography, localizing arterioles and mapping, etc.), understanding treatment indications and contraindications, what tools to use, safety conditions to be respected, methods of foam production, various injection procedures, monitoring, managing complications, follow-up, and writing out reports (38-40).

Pre requisites: mastery of duplex ultrasound technique and sclerotherapy, participation to practicals, tutoring.

How can this training be acquired?

- university teaching: national certificate of vascular medicine, DESC complementary certification of specialty in vascular medicine, possibly completed by a University diploma in phlebology.
- tutoring which requires making a list of experienced physicians willing to tutor colleagues wishing to train or to improve their technique..
- participating in workshops and meeting colleagues allows for a better understanding of the technique.
- participating in congresses, consulting bibliography, and CME.

In conclusion: quality training is mandatory to prevent incidents and accidents which could harm the patient, impair the technique's reputation, and that of physicians using it.

2/ EQUIPMENT.

The lists of equipment are given for information but are not exhaustive. They are likely to be modified according to technical innovations.

A/ manufacturing foam:

- a detergent sclerosing fluid: Polidocanol (Lauromacrogol) at 0.25%, 0.5%, 2%, and 3% or Tetradecyl sodium sulfate at 1 and 3% (41) (chromed glycerin does not foam).
- NaCl ampule at 0.9%.
- air, CO₂, or sterile oxygen.
- single use syringes (glass syringes are banned) 2 ml, 2.5 ml, 3 ml, 5 ml, 10 ml, and 20 ml with 3 parts (Terumo ®, BD ® or Braun ®) or with 2 parts (Discardit ®).
- a Luer Lock female-to-female connection Didactic ® or Vygon ®).
- a 3-way cock (Vygon ®).
- a sterile 0.2 micron air filter (Sterifix B Braun ®).
- equipment for the DSS method (Turbofoam ®): 0.2 micron filter (sterifix B Braun ®), a 3 way cock (Vygon ®), syringes with 2 parts.
- an Easyfoam ® device.
- a Sterivein ® device.

B/ injecting foam in ambulatory treatment:

- 21 G, 22 G, 23 G, 30 mm or 25 mm and rarely 26 G to 30 G needles.
- flexible extensions 20 cm Vygon ®, catheter 18 G (Intrasyte ® or Abbocath ®) 40 mm.
- butterfly (Microflex ®, Vygon ®).
- pulse color duplex ultrasound with at least a 7.5 to 10 MHz probe (ideal: 5 to 15 Mhz).
- sterile gel or spray chlorhexidin.

- disinfectant towels or sprays for US probes (without aldehyde which could deteriorate them).

C/ for the surgical block injection of great saphenous with a long catheter on empty vein:

- xylocaine® 1% bicarbonate buffer at 1.4%.
- a 5 F guide (Vygon ®).
- a 5 F Cook Royal Flush ® straight catheter for angiography.
- an Esmarch ® band.
- a Velpeau ® band.

D/ for other injection techniques:

- 20 G short catheter (Optiva Medex Medical ®).
- a long angiocath 4 F catheter (Super Torque ®, Johnson&Johnson Company ®, Cordis Europa ®).
- 1 mm outer diameter epidural anesthesia catheters (Vygon ®).

E/ for post treatment compression:

- for the great saphenous: class 2 tights or stockings (15 to 20mm Hg) or 3 (20 to 36mm Hg) class 2 or 3 (1 or 2 European standard), or superposition of 2 classes 2 (1+1 European standard), or superposition elastomousse ®/elastoplaste ®.
- for the small saphenous: socks class 2 or 3 French standard (1 or 2 European standard).
- or superposition elastomousse ®/elastoplaste ®, or other devices used to compress treated segments electively.

3/ MANUFACTURING THE FOAM.

A/ Material

The medical room hygiene must be excellent, the duplex ultrasound apparatus high quality, and resuscitation equipment immediately available.

Only sclerosing surfactant agents or detergents (Tetradecyl sodium sulfate, and Polidocanol, or Lauromacrogol) can be changed to foam. The concentration ranges from 3% for large segments to 0.20% for small varices (it is even weaker for telangiectasia). Microfoam should have a gas/fluid ratio ranging between 4 and 8 (below this value, foam is too liquid and lyses rapidly; above this value, it is weakly stable). The most commonly used ratio is 4 volumes of gas for 1 volume of sclerosing fluid. This optimal ratio is linked to the foaming agent (it is identical for the 2 available sclerosing agents) and not to the concentration of sclerosing agent. Thus, the proportion of gas should not be decreased in weak concentrations (42).

Plastic single use syringes are the safest. Silicone free syringes allow making a better quality foam because silicone, a lubricant, accelerates foam breakdown reducing its stability. It is possible to obtain stable foam at 0.10% with these syringes. It is important that various foam concentrations be available because varices, varicose networks, and sensitivity to sclerosing agents vary from one patient to the next. Nevertheless, using these double part syringes makes it more difficult to use a direct needle injection and usually requires using an indirect injection (butterfly or catheter). Foam must be prepared just before injection, whatever the manufacturing method or type of injection used.

B/ Methods.

There are at least 10 methods to manufacture foam (industrial: Cabrera, and office-made: Monfreux, Tessari, Sadoun, Garcia Mingo, Frullini, Gachet, Onorati, etc.).

The most commonly used office-made foam is Tessari's whirlpool (Irvine technique), it requires two syringes (non-silicone if possible), a female/female connector or a 3-way stop cock, and a sterile air filter. The alternative passage of the air/fluid mixture from one syringe to the other via a 3-way stop cock or a female/female connector will create foam. At least ten passages, the last ones under hyper pressure, are needed to create a homogeneous, stable, and compact foam for the best results.

Using an automated device (Turbofoam ®) creates a sterile more standardized foam. Specific kits (Easyfoam ®, Sterivein ®) also allow manufacturing sterile foam.

4/ INDICATIONS/CONTRAINDICATIONS.

Indications and contraindications are defined on clinical findings and duplex ultrasound examination, mandatory before any procedure.

A/ Indications.

They are clearly defined by the HAS. All patients at any stage of chronic venous disease (staged from C2 to C6 according to CEAP) may benefit from the technique (a varicose ulcer is not a contraindication for the treatment but the puncture/injection must be performed in healthy skin). This also applies to all varices, including diameters above 10 mm (43-44), saphenous trunks, saphenous tributary veins, pelvic, lymphoganglionar inguinal vein, perforating (by indirect injections), reticular, telangiectasia, venous malformations and recurrence after stripping, phlebectomy, CHIVA treatment, VNUS closure, laser and sclerosing therapy.

B/ Absolute contraindications (45):

- allergy to a sclerosing agent.
- severe systemic illness.
- acute deep venous thrombosis.
- obstructive post-thrombotic syndrome.
- severe lower limb arterial disease (stage III and IV).
- local skin infections.
- and only for Lauromacrogol which contains alcohol, Disulfiram treatment which is used for alcohol weaning.

C/ Relative contraindications:

- thrombophilia (requiring temporary anticoagulation with LMWH, FONDAPARINUX, or VKA).
- Known patent foramen ovale or aneurism of the interatrial septum (46-49) permitting the passage of foam into the left side of the heart (right to left shunt) at rest or following a Valsalva maneuver. even if no definitive neurological deficit or lesions are noted (brain MRI). Risk minimization should be applied: reduce foam volume, prolong the decubitus, and avoid Valsalva maneuvers.
- migraines with aura (50).
- Rendu-Osler disease.
- arterial and venous malformations.
- post treatment exposure to ultra-violet rays (sun or tanning machine).
- in the absence of studies excluding the risk, caution must be observed during confirmed pregnancy and breastfeeding period, by discussing the benefit /risk of a specific and exceptional indication with the patient's consent.
- the first 3 post-partum months are not indicated for foam treatment of varices.
- foam treatment is not indicated in the weeks following surgery.

- it is preferable not to schedule any surgery or long trip in the 2 months following the procedure.
- In case of cardio-vascular disease, preserving the superficial veins, which could be used for by-pass, should be considered.

D/ Remarks.

Anticoagulant and antiagregant treatments are not contraindicated (51)

Presenting with deep venous reflux is not a contraindication but an indication to screen for a post-thrombotic syndrome which could require temporary anticoagulation.

Varices of unusual size, shape, and localizations should lead to screening for possible arteriovenous fistula and post-thrombotic syndrome when varicose veins may act to bypass deep vein obstruction.

Very old age is not a contraindication for the procedure but injected foam volumes must be smaller.

Lymphedema treated by strong fitted compression is not a contraindication for the foam procedure.

5/ DUPLEX ULTRASOUND EXAMINATION.

3 are mandatory

A/ Initial patient assessment for the indication.

For a patient with superficial venous disease, duplex ultrasound examination, as a complement to clinical examination, must investigate arterial, deep and superficial venous networks as well as lower limb perforating veins to:

- screen for and assess arterial disease (SPI, ABPI),
- screen for acute venous thrombosis or sequels,
- describe the patient's disease,
- classify according to CEAP, including sub classification as appropriate,
- write out a detailed report of the varicose disease.

Ultra-sound examination data will help guide therapeutic decisions according to objectives: medical treatment, conventional or minimal surgery, or endovenous treatment (endolaser, radiofrequency or foam). The patient and his attending physician will be informed and consent will be given after a set period of time.

B/Mapping (52-54).

If foam treatment is indicated and accepted, allow adequate (legal time) time for patient reconsideration.

The duplex ultrasound is specific for this technique and has for goal to:

- accurately map the superficial venous system
- determine the most appropriate mode of injection: direct puncture, short or long catheter,
- determine the best site of puncture taking into account; vein caliber, tortuosity, presence of nearby arterioles, etc.
- determine the extent of the treatment and which veins are to be spared (including those which are hoped to become competent after an initial treatment 55-56), and draw their outline on the limb,
- calculate the theoretical volume (cross sectional area $\text{cm}^2 \times L \text{ cm}$) allow for decreased by spasm..
- choose the optimal concentration of the sclerosing agent according to: the size, depth, and the caliber of veins to be treated, modified by prior experience (to be increased in

case of initial failure, to be decreased in case of strong inflammatory reaction or previous hyper-pigmentation).

C/Echo guiding.

Ultrasound guidance is fundamental for the precision and safety of the technique. It includes:

- guiding of venous access with transversal and/or longitudinal views (depending on the individual preference). the tip of the needle must be visualized in the lumen but proving venous access by aspiration of low pressure dark blood is mandatory.
 - Monitoring foam progression allows for; the injection to be stopped immediately in case of extravasation, adjusting the volume injected and to monitor the effects of postural maneuvers and selective compression.
 - compression of the varix with the probe allows foam to reach the deep aspect of the vein and thus improve the destruction of all the endovein and rapid evolution of spasm.
- High quality foam and obtaining good spasm results in almost complete circulatory block of the varix, thus limiting its flow to the deep network.
- check the immediate effectiveness of the procedure, before removing the venous access. The vein should be in complete spasm and the residual lumen filled with foam.

6/ INJECTIONS.

A/ Site.

Puncture in the groin or the popliteal fossa should be avoided to prevent the most serious complication of the procedure which is intra-arterial injection.

For the GSV, except in specific cases, it is preferable to inject the saphenous trunk rather than the superficial tributary saphenous vein.

For the SSV, it is mandatory to locate accurately the SS artery (if present) so as to keep the injection site away from it.

In case of perforating veins, it is preferable not to inject in its trunk, because there is always a perforating arteriole nearby.

The puncture/injection is always performed after echo marking, preferentially in lateral decubitus the GSV, and ventral decubitus or kneeling position for the SSV (knee flexion decompresses the SSV). The decubitus ensures immobility and relaxation of the patient. Standing position should be avoided because of involuntary movements and possible vagal collapse.

B/ Direct puncture/injection (57).

Position of the operator:

- the injecting hand should rest on the patient's limb so as not to move during the injection,
- the other hand should hold the probe during the injection and the operator should be placed so as to keep in his field of vision: the syringe and the US screen. A probe holding device can be used so as to free one hand (58).

Choosing needle gauge: it is not recommended to use large needles (type IM, 21 G). The needle should be long enough to allow the syringe to bear on the skin and to have a tangential access to the vein so as to reduce the risk of extravasation during the spasm. The most commonly used needles are 25G, 0.5x16, 23G, 0.6x25 or 30, and 22G, 0.7x30.

C/ Indirect puncture/injection.

There are 3 methods, short catheter (cathlon), butterfly (59) and long catheter (60). The most appropriate puncture sites for short catheters are the mid third of the GSV and SSV.

- short catheter.

Raising the limb after access reduces the blood volume of the vein and so reduces foam required while improving contact with the lining of the vein. The foam volume needed to completely fill the femoral saphenous vein up to the junction is injected (usual volume of foam from 5 to 10 ml). If there is no spasm, an additional injection of 2 to 3 ml is required. Tourniquets can reduce spread of foam decreasing the passage of concentrated foam into the superficial tributary veins which will be treated later with lower concentrations via a butterfly. The risk of pigmentation is thus reduced.

- butterfly.

The best sites for short catheters are also the mid third of the GSV and SSV.

2 methods are used.

The butterfly may be introduced in the varix, blood reflux into the extension tube empties it of air (it can also be pre-filled with saline) before connecting the foam syringe and starting the US guided slow injection.

The butterfly can also be first connected to the syringe and the venous puncture can be performed after pre-filling the extension tube with foam. In this case also, it is mandatory to check for blood reflux in the extension tube and to have an echo-guided slow injection.

- long catheter.

For the GSV, the patient supine without any sedation. The venous access is performed either percutaneously: 5F Vygon®, or by cut-down under local anesthesia with Xylocaine 1%. The level of introduction is chosen according to the level of reflux, in the instep or more often under the knee.

A Cook Royal Flush F5® straight angiography catheter is inserted and advanced to 2 cm distal from the saphenofemoral junction in case of junctional valve reflux, and up to the preterminal valve if the terminal valve is competent. The catheter tip position is confirmed by US. An Esmarch band is wrapped around the limb from the ankle to the top of the thigh. Two milliliters of Polidocanol 1% microfoam are injected in the upper part under manual compression for 2 minutes. The catheter is then slowly withdrawn while continuously injecting the rest of the foam. The vein being empty and compressed, 4 to 8 ml of microfoam are enough to treat the GSV. The Esmarch band is kept on the limb for 5 minutes, then removed and replaced by two overlapped class 2 compression stockings (class 1 for European standard).

The residual varices will be treated during another session.

Whatever mode of injection is chosen, the injected foam volume should never exceed 15 ml per session and must be decreased for children, old patients, small size patients or in bad state of health, and in patients presenting with concomitant disease such as: atheroma-thrombosis, cardiac and respiratory insufficiency, large persistent foramen ovale, interatrial septum aneurism, Rendu-Osler disease, etc. The smallest effective volume is the best.

Intermittent compression maneuvers with the US probe allow to:

- distribute foam along varicosed segments to be treated,
- check the filling of these networks with echogenic foam,
- put the foam in contact with the deep aspect of the superficial vein wall.

The session is prolonged by putting on compression stockings (61) which the patient should not do by himself after treatment so as to prevent an accidental Valsalva maneuver which could in the presence of patent foramen ovale send bubbles into the general circulation. It is helpful if the compression stockings are applied before the session and turned down to the ankle for treatment. The patient should rest flat for a few minutes with their legs raised before progressively mobilizing. This minimizes the risk of vagal attack or migraine. The session always ends by walking so as to flush the deep venous network. No violent effort should be undertaken in the hours following the procedure but walking is recommended in the following days.

7/ FOLLOW-UP AFTER TREATMENT.

Follow-up can be scheduled 10 days after the procedure to assess early effectiveness and manage complications (induration, inflammation, residual pain, ecchymosis, pigmentation, matting, etc.). Duplex ultrasound examination should include screening for asymptomatic deep venous thrombus if found consider an immediate short course of anticoagulation and delayed screening for congenital or acquired thrombophilia.

Common femoral wall and/or popliteal thickening as well as convexity of a sclerous in the SFJ or SPJ should not be considered as DVT. Untreated persistent reflux is simply noted (complementary treatment would be premature).

Duplex ultrasound examination becomes mandatory and urgent when the patient has symptoms of DVT or PE, pain, skin discoloration, edema of the treated limb. Keeping telephone contact is thus required during treatment. Pain often comes from the sclerosis of perforating veins or of a gastrocnemius veins which does not require systematic anticoagulation treatment. Thrombectomy, thromboaspiration, local or general anti-inflammatory drugs, avoiding standing, walking, and checking compliance with wearing compression stockings will be sufficient to deal with these minor complications.

According to local protocol, US and clinical vascular check-up between the 4th and 12th week will allow assessment of clinical effectiveness (satisfaction, feeling, discomfort, relief, aspect, etc. which can justify, thrombectomy, thromboaspiration, NSAID, prolonged wearing of compression stockings), and duplex ultrasound (DVT, sclerous, persistent reflux, segments having regained continence which will not need to be treated), a complementary foam treatment may be performed or delayed (a sclerous may occur in a varicose vein several months after its injection).

Late follow-up (from 6 to 12 months) is mandatory in case of chronic venous disease which is progressive by definition. This allows an update of the patient's status (cosmetic and clinical), to perform another duplex ultrasound examination (absence of reflux, retractile fibrosis, or loss of varices proof of a good result or persistence of varicose reflux requiring complementary treatment).

At first, yearly follow-ups are required with possible complementary treatments. Then the frequency of check-ups will decrease except in the case of rapidly progressive chronic venous disease, chronic venous insufficiency, pregnancy, arteriovenous malformation, or post-surgical varicose neogenesis.

8/ COMPLICATIONS AND SAFETY.

The practitioner must be familiar with the diagnosis and management of all complications (62-63) and have the facilities to quickly implement an adequate treatment.

A/ Minor:

- ecchymosis, hematoma, pigmentations, matting (secondary onset of telangiectasia), vagal disorders, and anxiety are without serious consequence.
- migraine with aura. Preventive intake of an antimigraine drug for patients presenting with migraine. In case of PFO, reduce injected foam volumes to decrease the potential bubble load by extending decubitus, limiting Valsalva maneuvers after treatment, and mobilizing slowly will all help reduce the number and intensity of auras. A documented persistent and symptomatic large foramen ovale will require the consideration of an alternative therapy or a greater number of sessions and smaller injected volumes per session.

B/ Major:

- deep venous thrombosis must be screened for and treated early if found. Thrombophilic patients (history of thrombosis, documented genetic mutation or transitory coagulation disorder) must be treated preventively with anticoagulant drugs such as VKA, LMWH, or Fondaparinux.
- intra arterial injections require immediate hospitalization. Using duplex ultrasound and with good training this should be a very rare occurrence.
- anaphylactic shock remains exceptional but requires resuscitation. Associated signs are: generalized pruritus, edema, pallor, anxiety, cold extremities, blood pressure drop, and reactive tachycardia (which permits differentiation from vagal bradycardia). There are more allergic shocks with Tetracycl sulfate than with Lauromacrogol.
- the toxic reaction appears within thirty minute with a pseudo influenza syndrome associated to feeling bad, light fever, shivering, myalgia, lumbar pain, and hyper pigmented urine. These signs usually disappear within a few hours but, in very rare cases, the reaction can induce cardiac arrest. Using foam may decrease this risk by reducing the volumes of sclerosing fluids used.

Practical recommendations:

- the indication should be discussed in case of an underlying pathology (AHT, persistent symptomatic foramen ovale, allergies, etc.) and a anxious patient.
- preparing the patient: before anything else, the patient must be reassured and informed about procedure so as to prevent anxiety and vagal disorders. The patient does not need to change his diet and fasting is not necessary. An anxiolytic or an antihistaminic as well as applying a local anesthetic (spray or unguent EMLA ®) may be useful for anxious patients. Patients with migraine can take a prophylactic treatment before the procedure.
- installing the patient: vagal disorders occur mostly during examination while standing (assessment or mapping). The patient must be comfortably positioned so he will not move during the procedure (decubitus) or risk having a vagal disorder. The session ends with resting for a few minutes in the supine position and progressively getting up, then walking.
- asepsis: performing the puncture in an infected cutaneous area is contraindicated. Disinfecting the injection site is performed by swabbing with an antiseptic agent. It is mandatory to use sterile single use material (syringes, needles, connections, etc.) and a sterile mono-dose US gel or even better spray chlorhexidin.
- puncture/injection: the puncture performed with a needle or a catheter must be intravenous and the injection should be slow and painless. US guidance should limit the risk of extravasation which when observed requires immediate stopping of the injection.
- the patient should limit Valsalva maneuvers after the injection especially when putting on the compression stockings and when getting up.
- practicing a violent sports is not recommended in the hours following treatment but walking is advised.
- Antibio prophylaxis (Amoxicillin) for infectious endocarditis may be discussed in case of cardiac valve pathology or replacement.
- The emergency kit should include at least: an oxygen mask, an insufflation balloon, a Guedel airway, oxygen, adrenaline, injectable and inhalable corticosteroids, a nitrous derivative, an infusion catheter, and intravenous fluids for volume replacement (64).

9/ REPORTS AND FRENCH LEGAL ASPECTS.

A minimal legal background should be defined so as to offer legal protection for treatment by foam injection in saphenous veins and their incontinent tributaries (65-68).

Obligations and guarantee of the physician opposable to the patient:

- be a doctor in medicine, and member of the French Board of Physicians.
- certified in vascular medicine (certification in angiology or qualification acknowledged by the French Board of Physicians) or any equivalent theoretical and practical training.
- be trained in US, phlebology, with specific training in echo-guided sclerotherapy. After obtaining the patient's consent, the procedure may be performed in a medical office, by a medical student if he is tutored by a qualified physician and under his responsibility.
- open and document a medical file for the patient including reason for consultation, and relevant history which could interfere with the surgery (venous thrombosis, thrombophilia, allergies), and inclusion or exclusion criteria.
- explain the benefit/risk with loyal and informative information, by proposing possible alternatives: abstention, compression, conventional surgery (stripping) or an alternative (laser, Venous closure, etc.) by specifying to the patient that there is no scientific validation *stricto sensu*, in any referential published by the HAS.
- explain that this treatment has for aim to "manage" chronic venous disease but cannot cure it definitively since it is progressive.
- explain to the patient that concomitant emergence of an underlying disease (coronary insufficiency leading to infarct for example) is not necessarily due to foam treatment.
- explain that the methodology, its modalities, its advantages, and inherent constraints.
- explain to female patient that pregnancy is not advised during treatment and in the 2 following months. Likewise, planned surgery and or a long trip superior to 6 hours are not advised during that period.
- give the patient a more than fifteen-day delay allowing to accept or refuse treatment.
- obtain the patient statement that he will observe recommendations.
- inform the patient about the cost and limits of reimbursement. In France, a written estimation is mandatory when the total cost of a session is superior to 70 €
- offer follow-up with a phone contact in case of minor or major adverse events.
- write out and give reports: initial assessment, operation report, check-up assessment, copies for the attending physician, and a sheet of recommendations.

Addendum 1

INFORMATION ON ECHO-GUIDED FOAM TREATMENT OF VARICES.

Based on guidelines for endovascular treatment of varices by echo-guided injections of fibrosing foam: the Grenoble consensus. Version 2007.

Please check the site: la-mousse.com for more detailed information.

You are going to benefit from a phlebology treatment, intended to improve venous circulation (does not apply to telangiectasia or varicosity, very small varices less than 1 mm in diameter which are only a cosmetic problem).

You present with lower limb superficial venous insufficiency with at the level of varices: loss of wall elasticity and reactivity along with deterioration of valves meant to prevent downward blood reflux in the standing position. The result is an increased pressure in the varicose veins which may trigger pain, lower limb heaviness, cramps, and bloating of legs (edema).

In some cases, skin deterioration is observed which may induce a chronic wound (varicose ulcer). More rarely, the dilated vein (varix) may rupture after trauma or sometimes spontaneously (hemorrhagic varicose vein rupture). Finally, blood stagnation in the varices induces the formation of a clot (superficial venous thrombosis also called superficial phlebitis previously called periphlebitis).

The aim of the treatment is to slow the evolution of chronic venous disease by repairing or eliminating varices which no longer play their role in blood return to the heart. Venous return is improved by relieving the important deep network of healthy veins. Echo-guided injection of a sclerosing foam (AETOXISCLEROL or TROMBOVAR) in the varix triggers inflammation of the venous wall leading to its fibrosis. This decreases the caliber of the vein and allows the blood to flow freely upward or, most of the time, blocks it completely and redirects the flood to the numerous healthy veins which will bring it up. Fibrosis, consequence of foam injection, concerns the varix wall (container) and must be differentiated from thrombosis or phlebitis, which is the consequence of blood coagulation with formation of clot (content).

The expected clinical benefits are: decrease of pain, feeling of heaviness, edema and skin disorders but also cosmetic improvement.

Immediate complications are usually without consequence.

It can be dystonic reactions (linked to stress) and migraine with aura (linked to the injected product) which present as neurological disorders, often vision, headaches, feeling of respiratory oppression with a light reflex cough, tingling in the extremities of hands and legs, toneless legs, etc. General vagal disorders are managed by keeping the patient lying down with legs elevated for a few minutes.

Immediate severe complications are extremely rare.

An allergic shock and a toxic reaction may be potentially lethal (you must report any allergy before the procedure: drug, insect bite, contact, etc.).

Tissue necrosis often leaves esthetic and functional sequels. It is most often a consequence of arterial injection.

Late reactions may occur (after 8 to 10 days).

Most of the time it is venous induration (sclerosis means « to harden» in Greek), which can induce a slight discomfort on palpation but it is sometimes pain which will be relieved by an anti-inflammatory unguent, by an anti-inflammatory analgesic cataplasm,

and more rarely by an oral pain-killer (antalgic, anti-inflammatory, etc.). This transient phenomenon of hardening is actually expected and shows the effectiveness of treatment. Ecchymosis and hematoma resolve spontaneously.

Pigmentation (brown marks on the path of treated veins) almost always resolves in time. Matting, growth of small varices called telangiectasia, may be treated secondarily by complementary micro sclerosing.

Phlebitis or DVT (formation of a clot inducing pain, swelling, and hyperthermia of a limb) is rare. Its onset is fostered by sedentariness and a little documented predisposing state called thrombophilia. It is an indication for a rapid initiation of a transitory anticoagulant treatment. You must thus report any history of phlebitis.

Skin necrosis or ulceration is extremely rare but healing is slow and sometimes leaves a scar.

You must contact your physician immediately in case of abnormal reaction to treatment.

To prevent complications, you must report your allergies, history of thrombosis (phlebitis or pulmonary embolism), and cardiac history (persistent foramen ovale, aneurism of the interatrial septum, endocarditis, valve disease or replacement, angina, myocardial infarction, cardiac rhythm disorders, etc.).

Pregnancy and breast feeding are not advised during the treatment. Likewise, planned surgery and or a long trip superior to 6 hours are not advised during that period.

Before deciding to undergo foam treatment, it is important to assess the benefit/risk ratio with your physicians.

Addendum 2

CONSENT FOR THE PROCEDURE OF ENDOVENOUS FOAM TREATMENT OF VARICES.

When consulting onwith Doctor I was clearly informed about the advantages and risks of this treatment. I was able to freely ask all questions which I deemed useful and I completely understood the answers which were given.

I give my fully conscious informed consent for this procedure after having been completely informed.

At..... On

Signature of the patient:
physician

Signature of the
