Guidelines for Diagnostics and Treatment of Venous Leg Ulcers

Developed by the Guideline Subcommittee of the
European Dermatology Forum

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No conflicts

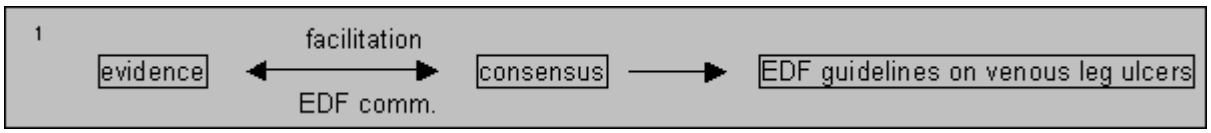
GENERAL

The need for European guidelines in dermatology is indicated by the ongoing development in European dermatology. The EDF, the EADV and the ESDR headed by the UEMS, also officially approved by the European Community, form the structure of pan European dermatology. The European guidelines differ substantially from individual national guidelines. The main differences are:

a. No restrictions by different national regulations.

b. No restrictions imposed by local rules on drug distribution, re-embursement facilities, etc.

The diagnosis and treatment of venous leg ulcers is an important item within all European dermatological departments. Although this is not exclusive for this particular speciality, phlebology surgeons, physicians interested in vascular medicine and general practitioners also treat patients with venous leg ulcers.
However, the most difficult cases are treated by dermatologists.
The European Dermatological Forum has therefore decided to produce a European guideline on this subject. The process went as follows[1]:



INTRODUCTION

This guideline on the management of venous leg ulcers has been prepared by the guidelines committee of the European Dermatological Forum (EDF) and based on the already existing guideline prepared by the Dutch Society for Dermatology and Venereology. It presents evidence-based guidance for treatment, identifying the strength of evidence available at the time of preparation of the guideline, and a brief overview of epidemiological aspects, diagnosis and investigation (level S3).

Aim

This guideline is a document with recommendations and management instructions supporting the daily practice whereby the optimum treatment (especially healing and prevention of recurrence) of the patient is central. The guideline is based on the results of scientific research and contiguous opinions directed at explicating good medical practice. The document is intended as a guideline for the everyday diagnostics and treatment of venous leg ulcers by dermatologists or other medical specialists.

Problem description and initial questions

Questions regarding the diagnostics, the treatment, the follow-up treatment and the organization of care of venous leg ulcers were answered for the purpose of developing the guideline.

Working group

The Commission on guidelines of the European Dermatological Federation (EDF) inaugurated the Chairman of the working group on wound healing during its annual meeting in January 2004.
This guideline is the first on wound healing and covers the subject of venous leg ulcers.

Scientific basis

The guideline is based as much as possible on proof provided in published scientific research. Relevant articles were looked for via systematic search, carried out in Medline, Cochrane and Cinahl databases from 1995 to 2006. Previously searched literature was used for literature prior to 1995. Hereby, it must be remarked that evidence-based medicine started relatively late in Phlebology. This means that much of the Anglo-Saxon literature is a repeat of the earlier efforts (at international meetings) published in French, German, Swiss, Italian or Spanish literature.
In addition to the articles found via literature search, articles were extracted from requested list of references. Articles that remained after selection by the members of the working group are cited as the basis for the various conclusions. The selected

articles were subsequently assessed on the quality of the research and were graded for the strength of proof by the members of the working group. The classification that was used hereby is shown in Table I.
One may consider that European references, especially in German and French, are underestimated compared to those from North America due to the of lack of papers cited in PubMed / M/code in the field of phlebology.
The assessment of the various articles can be found in the different texts under the heading "***scientific basis***". The scientific proof is then briefly summarized in a ***conclusion***. The most important literature, including the ***strength of proof*** on which this conclusion has been based, is mentioned in the conclusion. Since evidence-based medical (EBM) publications are limited - in this journal - in a field in which it is hard to recruit enough and comparable patients - no improvement in the treatment of leg ulcers may be achieved, especially with surgical techniques (think of paratibial fasciotomy, etc.). Therefore, the experience of experts is essential, and the "recommendation" is a good way to present it (Level D).
For a recommendation, besides the scientific proof, often other aspects such as patients' choices, costs, availability (in various echelons) of organizational aspects are important. These aspects are mentioned under the heading "***other considerations***". The ***recommendation*** is the outcome of the available proof and other considerations.
Following this procedure increases the transparency of the guideline. It offers room for an efficient discussion during the meetings of the working group and moreover increases the clarity for the user of the guideline.

For articles concerning: intervention (prevention or therapy)

A1 Systematic reviews of at least several studies of A2-level, whereby the results of individual studies are consistent.

A2 Randomized comparative clinical study of good quality (randomized, double blind controlled trials) of adequate size and consistency.

B Randomized clinical trials of moderate quality or inadequate size or other comparative study (not randomized, comparative cohort study, patient-control-study).

C Non-comparative study.

D Opinion of experts, for example, the members of the working group.

For articles concerning: diagnostics

A1 Study into the effects of diagnostics on clinical outcomes in a prospectively followed well-defined patient group with a previously defined policy on grounds of the to be investigated test results, or decision study into the effects of diagnostics on clinical outcomes, whereby results of study of A2-level are used as a basis, and adequate consideration has been given to mutual dependence of diagnostic tests.

A2 Study in light of a reference test, whereby criteria have been defined beforehand for the investigation test and for a reference test, with a good description of the test and the studied clinical population; it must concern an adequately large series of consecutive patients and must make use of pre-defined cut-off values, and the results of the test and the 'golden standard' must have been assessed independently. In situations in which multiple, diagnostic tests play a role, in principle, a mutual dependence and the analysis should be adjusted to this, e.g. with logical regression.

B Comparison with a reference test, description of the investigated test and population, but excluding the characteristics that are mentioned further in A.

C Non-comparative study.

D Opinion of experts, for example, members of the working group.

Level of the conclusions

1 One systematic review (A1) of at least 2 independently conducted studies of level A1 or A2.

2 At least 2 independently conducted studies of level B.

3 One study of level A2 or B or a study of level C.

4 Opinion of experts, for example, the members of the working group.

Legal significance of guidelines

Guidelines are not legal regulations, but "evidence-based" insights and recommendations, which should be satisfied by the care providers in order to provide good quality care. Considering that these recommendations are mainly based on the "average patient", the care providers may, if required, deviate from the recommendations on the basis of their professional autonomy. Deviation from the guidelines is necessary if the situation of the patient requires it. Any deviation from the guideline should be based on arguments and should be documented.

Revision

The client / responsible authority will determine at the latest in 2010 whether this guideline is still valid. If required, a new working group is inaugurated for the purpose of revising the guideline. The guideline will become invalid if new developments make revisions necessary.

CHAPTER 1. Epidemiology, Etiology and Symptomatology

1.1 Epidemiology

A venous leg ulcer is a defect in pathologically altered tissue on the lower leg on the basis of chronic venous insufficiency (CVI). CVI is a symptoms complex based on an inadequate venous return, which leads to a decompensation of the venous and microcirculatory function. Chronic venous ulceration is the severest manifestation of this disorder[1]. A venous ulcer with no tendency to heal within 6 weeks to 3 months or that has not healed within a year after optimum phlebological therapy is designated as therapy resistant[2]. About three-quarters of all leg ulcers are generally considered to be mainly of venous origin[20].

Epidemiological data is more difficult to interpret than expected at first sight because of methodological differences. It makes a big difference whether a whole population, a particular group of individuals in a certain region or a patient population is investigated. The manner of registration also influences the outcome. Even filled-out polls, polls filled out by an investigator, special questionnaires on the presence of ulcers and whether or not a physical examination was conducted all have a considerable influence on the results[3].

In German studies, the prevalence of venous ulcers was reported in 1% in the population, and in 4-5% of those individuals older than 80 years[2]. This was in keeping with the findings that 1-2% of the adult population either has or had a venous ulcer[4,5]. In the western countries, a prevalence of active venous ulcers in the general population older than 18 years was reliably estimated to be at 0.3%[5,6]. An ulcer is encountered 2 to 3 times as often in women of all age groups[7]. There is a clear increase with age. Chronic ulcers below the age of 60 years are unusual[1]. The prevalence among the elderly may be quite high (12.6% of leg ulcers (C5-C6) in a Swedish rural population older than 70 years[17]. However, up to 50% of leg ulcers are caused by superficial venous insufficiency[18,19].

The prevalence of active and healed ulcers together is about 1%[1]. The prognosis is not very good. About 50% of the treated ulcers had healed within 4 months[1], about 20% had still not healed after 2 years and about 8% had not healed after 5 years[5,6]. The annual recurrence was 6-15%[6]. The total risk of recurrence was about 3-15%[1] and the risk of recurrence within the first year was 30-57%[2]. The majority of the ulcers recurred at least once[1]. Carpentier et al reported no significant difference between the prevalence of varicose veins in different areas in France[14], but noted a consistent difference between sexes; 50.5% of those affected were women and

30.1% were men. No data was available on leg ulcers.

1.2 Etiology

Venous insufficiency was noted to be the most important cause in a large number of venous ulcers. Moreover, arterial insufficiency, diabetes mellitus, vasculitis, malignancy, infections and other less frequent causes for ulceration may accompany venous disease.
In a large number of cases, long-term complications of deep venous thrombosis, the so-called post-thrombotic syndrome, causes CVI. Estimates vary (as do the used definitions), but on average, 1 in 3 patients who suffer from a deep venous thrombosis develops post-thrombotic complications in the subsequent 5 years. The chance of developing CVI after a thrombotic leg is lower when medical elastic compression hosiery (MECH) is worn[8,9].
There are different mechanisms for pumping the blood effectively against the pull of gravity. The cooperation between the venous valves and the calf muscle pump is the most important factor. The blood is pumped towards the heart while walking, whereas the valves prevent backflow. As a consequence, the venous pressure drops when the person is walking. A reflux of the blood occurs when this mechanism fails (in upright position) and an increased pressure develops in the veins of the lower legs (increased ambulatory venous pressure or venous hypertension).
First of all, varices will develop because of the increased venous pressure. The venous pressure will also increase in the venules and in the capillaries upon further decompensation. As a result of this increased intra-capillary pressure, the capillary filtration fraction will increase and edema will develop because of the leakage of fluid. Besides the leakage of fluid, there is also a leakage of high molecular weight substances such as fibrin. This can be demonstrated as a "cuff" around the capillaries. Initially, the thought was that these fibrin cuffs formed a barrier for the diffusion of oxygen resulting in local anoxia and ulceration[10]. However, this theory was refuted by the fact that fibrin cuffs around capillaries have been demonstrated in other skin diseases without any disturbance in the transcutaneous oxygen tension. The trapping of leukocytes in the capillaries and the release of free radicals have also been proposed as a possible explanation[11]. Furthermore, the transmission of high venous pressures to the dermal microcirculation results in the stimulation of an inflammatory process in which cytokine and growth factor release leads to leukocyte migration into the interstitium and the triggering of further inflammatory events. This process is associated with the intense dermal fibrosis and tissue remodeling seen in chronic venous insufficiency[22].
In capillary microscopy, thrombus formation in the capillaries of the skin was not only observed in white atrophy lesions but also in other cutaneous manifestations of CVI. This was also proposed as an explanation for the ulceration. Finally, it was demonstrated that the fibrin cuffs around the venous leg ulcer do not capture oxygen, but probably growth factors, so that these are less active in the wound.
In spite of all these hypotheses, the exact mechanism of the skin abnormality and ulceration still remains obscure.

1.3 Symptomatology

The venous leg ulcer arises either "spontaneously" or often after a minor trauma. The complaints of the patient as a result of the ulcer may vary from less pronounced to very pronounced. Venous leg ulcers can be painful. The complaints of pain may be prominent in the ulcerative phase of white atrophy or if accompanied by other factors such as an infection.
Clinically, venous leg ulcer is a part of CVI. Patients with CVI develop various skin abnormalities over a period of time. The percentage of patients who develop symptoms remains unknown because it has never been properly mapped.
The venous ulcer is generally located on the medial or lateral side of the ankle[4]. A particular form is the ulceration in acroangiodermatitis[2] of the forefoot. If the ulcer is located on another part of the lower leg, then one must strongly suspect that causes other than venous insufficiency play a role.
The clinical characteristics of CVI are generally known. For the sake of completeness they are mentioned here once again: varicosity, edema, corona phlebectatica, hyper-

pigmentation, dermato-et liposclerosis, white atrophy and the ulcer[12] . Stasis dermatitis is a manifestation of CVI.
The changes in the skin in venous insufficiency are a result of changes in the macro- and microcirculation. It is unclear why in one patient an extensive dermato-et liposclerosis is formed, whereas in another patient white atrophy is prominent. Local factors possibly play a role in this. This should be investigated further.

1.4 Quality of life

Venous ulcers have a substantial impact on patients' lives and affect most issues of health-related quality of life (HRQOL) such as bodily pain, health transition, mental health, social functioning and vitality[21]. Treatment, and especially healing of venous ulcers, results in a significant improvement in these areas. Nonetheless, a few specific HRQOL instruments have been developed. Studies indicated that these instruments were suboptimal and that generic instruments such as the SF-36, SF-12 and EuroQoL-5D are recommended for the purpose of measuring the impact on patients' lives, for time being[16].

Literature

1. The Venous Forum of the Royal Society of Medicine and Societas Phlebologica Scandinavica. The management of chronic venous disorders of the leg: an evidence-based report of an international task force. Phlebology 1999; 14 Suppl 1:23-5.
2. Korting HC, Callies R, Reusch M, Schlaeger M, Schöpf E, Sterry W. Dermatologische Qualitätssicherung. Leitlinien und Empfehlungen München 2000; 202-10.
3. Krijnen RMA, de Boer EM, Bruynzeel DP. Epidemiology of venous disorders in the general and occupational populations. Epidemiol Rev 1997; 19:294-309.
4. Callam MJ, Ruckley CV, Harper DR, Dale JJ. Chronic ulceration of the leg; extent of the problem and provision of care. Br Med J (Clin Res Ed) 1985; 290:1855-6.
5. Guidelines for the diagnosis and therapy for diseases of the veins and lymphatic vessels: Evidence-based report by the Italian College of Phlebology. Int. Angiology 2001; 20 Suppl 2:1-73.
6. Nicolaides AN. Investigation of Chronic Venous Insufficiency: a consensus statement.
Circulation 2000; 102:123-63.
7. The Alexander House Group Consensus paper on venous leg ulcers. Phlebology 1992; 7: 48-58.
8. Brandjes DP, Buller HR, Heijboer H, Huisman MV, De Rijk M, Jagt H, et al. Randomised trial of effect of compression stockings in patients with symptomatic proximal-vein thrombosis. Lancet 1997;349:759-62.
9. Prandoni P, Lensing AW, Cogo A, Cuppini S, Villalta S, Carta M, et al. The long-term clinical course of acute deep venous thrombosis. Ann Intern Med 1996;125:1-7.
10. Browse NL, Burnand KG. The cause of venous ulceration. Lancet 1982;ii: 243-5.
11. Coleridge Smith PD, Thomas P, Scurr JK Dormandy JA. Causes of venous ulceration: a new hypothesis. Br Med J 1988; 296:1726-7.
12. Philips T, Stanton B, Provan A, Lew R. A study of the impact of leg ulcers on quality of life: financial, social and psychological implications. J Am Acad Dermatol 1994;31:49-53.
13. Rabe E, Pannier-Fischer F, Gerlach H, Breu FX, Guggenbichler S, Zabel M. Guidelines for sclerotherapy of varicose veins. Dermatol Surg. 2004;30: 687-93.
14. Carpentier PH, Maricq HR, Biro C, Poncot-Makinen CO, Franco A. Prevalence,

risk factors, and clinical patterns of chronic venous disorders of lower limbs: a population-based study in France. J Vasc Surg. 2004; 40: 650-9.

15. Charles H. Does leg ulcer treatment improve patients quality of life? J Wound Care 2004; 13: 209-13.
16. Iglesias CP, Birks Y, Nelson EA, Scanlon E, Cullum NA. Quality of life of people with venous leg ulcers: a comparison of the discriminative and responsive characteristics of two generic and a disease specific instruments. Qual Life Res. 2005; 14: 1705-18.
17. Marklund B, Sulau T, Lindholm C. Prevalence of non healed and healed chronic leg ulcers in an elderly rural population. Scand J Prim Health Care 2000; 18: 58-60.
18. Tassiopoulis AK, Golts E, Oh DS, Labropoulos N. Current concepts in chronic venous ulceration.
Eur J Vasc Endovasc Surg. 2000 Sep;20(3):227-32.
19. Bergan JJ, Schmid-Schonbein GW, Smith PD, Nicolaides AN, Boisseau MR, Eklof B. Chronic venous disease. N Engl J Med. 2006 Aug 3; 355(5): 488-98.
20. Chaby G, Viseux V, Ramelet AA, Ganry O, Billet A, Lok C. Refractory venous leg ulcers: a study of risk factors. Dermatol Surg. 2006 Apr; 32(4): 512-9.
21. Kahn SR, M'lan CE, Lamping DL, Kurz X, Berard A, Abenhaim LA. Relationship between clinical classification of chronic venous disease and patient-reported quality of life:
Results from an international cohort study. J Vasc Surg. 2004; 39: 823-8.
22. Nicolaides AN.Chronic venous disease and the leukocyte-endothelium interaction: from symptoms to ulceration. Angiology. 2005 Sep-Oct;56 Suppl 1:S11-9.

CHAPTER 2. DIAGNOSTICS

The differential diagnosis of the crural ulcer is large. Still, there are several diagnoses that can be said to occur the most frequently. It is essential to immediately establish a correct diagnosis as adequately as possible, considering that different diagnoses have totally different approaches and treatments. An incorrect diagnosis may have dramatic consequences for the patient in several situations[1].

2.1 Anamnesis

Scientific basis

A good anamnesis is indispensable. Many patients with a crural ulcer have an extensive previous medical history and comorbidity. Good studies into the value of specific items for the anamnesis are lacking.

Conclusion

Level 4	Good studies on the value of specific items for anamnesis are not available. Nevertheless, a good anamnesis is indispensable. Level D

Other considerations

Field experience and consensus within the various disciplines indicated that the previous medical history as well as the family anamnesis and the specific aspects of the ulcer must be dealt with extensively in the anamnesis (see Table).

Subject	*Anamnesis*

Previous medical history	Varicosity and treatment of varices
	Venous thrombosis
	Leg ulcer
	Peripheral arterial vascular disorder (including complaints of intermittent claudication)
	Diabetes mellitus
	Rheumatoid arthritis
	Extensive leg trauma
	Medication use
	Mobility and nutritional status
Family anamnesis	Varicosity
	Venous thrombosis
	Leg ulcers
	Vascular disorder
Specific aspects	Duration of the ulcer
	Pain
	Previous treatment
	Fever and other symptoms of infection
	Agility of the ankle joint

Recommendation 1

The working group recommends that the previous medical history, family anamnesis and specific aspects are dealt with extensively during the anamnesis (see Table).

2.2 Physical examination

The international CEAP classification was designed to obtain an unequivocal description of the abnormalities in patients[2]. This classification was revised in 2004[53]. The physical examination is the leading feature in this classification.

C	E	A	P
Clinical status (clinic)	Etiology	Anatomy	Pathophysiology
C0 no visible abnormalities	E_p primary	A_s superficial	P_r reflux
C1 teleangiectasias or reticular veins	E_s secondary	A_p perforating	P_o obstruction
C2 varices	E_c congenital	A_d deep	$P_{r,o}$ reflux and obstruction
C3 edema	E_n no venous cause identified	A_n no venous location identified	P_n no venous pathophysiology identified
C4 Changes in skin and subcutaneous tissue secondary to CVD			
C5 healed ulcer			
C6 active, open ulcer			
S symptomatic, including ache, pain, tightness, skin irritation, heaviness, and			

muscle cramps, and other complaints attributable to venous dysfunction			
A asymptomatic			

Recommendation 2

The working group recommends the use of CEAP classification for physical examination. In addition, the size, site and characteristics of the ulcer should be recorded.

2.3 Supplementary investigation

2.3.1 Venous investigation

Venous Doppler

Scientific basis

Doppler sonography is a simple, practical and cheap technique for the diagnosis of venous reflux.
Comparative studies have mainly been done with descending phlebography, duplex diagnostics and venous pressure measurements. The sensitivity and the specificity of Doppler diagnostics in uncomplicated varicosis of the greater saphenous vein (GSV) and the saphenofemoral insufficiency are high (>92%). However, the sensitivity and especially the specificity are clearly lower in case of the recurrence varicosis of the GSV, or in reflux in the fossa poplitea and in venae perforantes (<70%)[3-6]. Besides, Doppler diagnostic strongly depends on the investigator. The value of the Doppler diagnostic is doubtful considering that in a considerable number of cases of venous leg ulcers there is an insufficiency in the deep venous system or an insufficiency in the venae perforantes.

Conclusion

Level 2	Doppler has a low sensitivity and a low specificity in the diagnostics of the deep venous system and the venae perforantes. *B* *Raju 1990[3]; McMullin 1992[5]; Rautio 2002[6]*

Recommendation 3

The use of Doppler in the diagnostics of venous leg ulcer is not advised for routine investigation of the deep venous system and the venae perforantes.

Venous Duplex

Scientific basis

Duplex ultrasonography is a combination of B-mode echography and Doppler sonography. The technique was initially utilized for the diagnostic of deep venous thrombosis. It was Van Bemmelen who, towards the end of 1980s, demonstrated that the diagnostic of varices and venous insufficiency could be conducted reliably with duplex[7]. One could look at the diameter, the duration of the reflux, the presence of flow and the compressibility of the vein.
The duration of the reflux in normal proximal veins of the leg is <1 sec. and <0.5 sec. in the distal veins[8]. There is no clear demonstrable difference between the induction of the reflux signal (in the proximal deep veins) between the classic Valsalva maneuver and the "rapid cuff inflation"[9]. The former is preferred, considering its simplicity.
Similarly to Doppler, the diagnostic strongly depends on the investigator. The

variation coefficient of the reflux measurements is considerable (30-45%), but the inter-observer reliability is good (kappa 0.86) if the above-mentioned cut-off points of the reflux are strictly adhered to.
Although it is difficult to correlate Duplex to another technique, comparative studies on clinical investigation, venous pressure measurements, plethysmographic techniques and descending phlebography were conducted. The best correlation was found using descending phlebography, which demonstrated a sensitivity of 79-100% in investigations into reflux in the deep system. The specificity was clearly lower (63-88%)[10].
Duplex scanning for the detection of deep venous insufficiency correlated well with descending phlebography. The sensitivity (79-100%) was good, but the specificity (63-94%) was somewhat lower[11]. CEAP classification can be established only if Duplex has been performed.

Conclusion

Level 2	It has been demonstrated that duplex diagnostic has high sensitivity and specificity in the diagnostics of the superficial and deep venous system of the legs. *A2* *Baker 1993*[10] *B* *Masuda 1992*[11] *C* *Magnusson 1995*[4]

Other considerations
A disadvantage of the duplex diagnostics is that there are patients on whom the technique may be laborious to carry out because of mobility problems. However, the investigation is less burdensome for the patient, relatively cheap and may be repeated easily. Furthermore, duplex diagnostic is the standard venous investigation, which allows further classification of chronic venous insufficiency and classification-related treatment.

Recommendation 4

Duplex investigation is the preferred technique for patients with a venous leg ulcer.

Scientific basis
Phlebography is a radiological technique in which contrast fluid is injected into the venous vascular system. A distinction between ascending phlebography and descending phlebography is made. In the ascending phlebography, contrast fluid is injected into a vein in the back of the foot, whereas in the descending phlebography, the contrast fluid is injected into the femoral vein, after which a Valsalva maneuver is performed. Descending phlebography has been compared with deep venous pressure measurements. The sensitivity was good (70-100%), but the specificity was relatively low (40-75%)[3].
Duplex diagnostic has largely replaced phlebography. However, phlebography may still be valuable in distinguishing between primary and secondary varices, in identifying the level of obstruction in the femoral and the iliac veins, in detecting incompetence of the gastrocnemius veins and in determining the level of reflux in the deep venous system as well as the status of the valves.

Conclusion

Level 2	Descending phlebography has a high sensitivity but a low specificity for specifying venous incompetence. *B* *Raju 1990*[3]

Other considerations
The investigation is burdensome for the patient and is expensive.

Recommendation 5

Descending phlebography is not the diagnostic of (first) choice for a leg ulcer. The technique should be used only on indication. The sensitivity is then high.

Direct venous pressure measurement

Scientific basis

An increased ambulatory venous pressure causes venous pathology. There is a clear correlation between this pressure and the extent of pathology[12]. This pressure can be invasively measured directly by means of a cannula in a superficial foot vein. There is a good correlation between this pressure in a foot vein and the pressure in the deep veins at the ankle height[13]. Superficial venous insufficiency can be distinguished from deep venous insufficiency by occluding the superficial system by means of a tourniquet[14]. The direct venous pressure measurement is seldom used because of its invasive character and the fact that the procedure is complicated.

Indirect venous pressure measurement

Scientific basis

Strain gauge plethysmography was already described by Whitney in 1953 and was developed further into a method for measuring venous pressure indirectly by Brakkee and Vendrik in the 1960s[15,16]. This method was developed further for the purpose of measuring the venous pressure indirectly in the 1990s, by Van Gerwen - whereby the complete measurement was carried out while the patient was lying down[17]. The method was validated by Janssen, who demonstrated a good correlation with directly measured venous pressure[18].
In this so-called "lying position" pump function test, volume changes in the legs were measured using a mercury strain gauge.
An increase in venous pressure such as that in the upright position is simulated with the help of a pressure cuff on the upper legs. This increase in pressure is accompanied by an increase in the venous volume. When the maximum increase has been reached, standardized calf muscle exercises are performed whereby the calf muscle pump pushes the blood through the cuff towards the heart. The mercury strain gauge again registers the decrease in the volume as a result of the calf muscle pump.
The decrease in volume is accompanied by a decrease in pressure. The measured decrease in volume can be calculated into a decrease in pressure by determining a pressure-volume relationship.
The decrease in pressure is a good measure of the function of the calf muscle pump of the deep veins.
This method is not used much because a good commercial version is not yet available. Moreover, the investigation is time-consuming and can only be carried out in a mobile and cooperative patient.

Photoplethysmography

Scientific basis

The principle of the photoplethysmography, whereby the transmission of light through the skin is measured as a measure of the change in blood volume in the skin, was already described in 1937 by Herzman[19]. This technique was initially used for arterial investigation, but was modified for venous investigation by Abramowitz in 1979[20]. The technique was further developed into a standardized digital version by Wienert and Blazek in the 1980s[21,22].
The measurement is generally done in the sitting position with a measuring probe fixed to the medial side of the lower leg above the ankle, whereby standardized calf muscle exercises are performed. The volume of blood in the skin under the probe is measured.
The most important parameter of the photoplethysmography is the venous refill time. There is a good correlation between the refill time measured with direct venous

pressure measurement and with photoplethysmography[19,23].
However, the relationship between the refill time and the level of venous insufficiency is not good[24,25].
The influence of the superficial venous system on the refill time may be eliminated using small pressure cuffs when the refill time is short. A clear increase in the refill time after occlusion of the superficial varices indicated a good deep venous function. Unfortunately, the measurements did not lend themselves well for interpretation[26].

Other plethysmographic methods for venous investigation

Scientific basis
Volume changes may also be measured with air plethysmography and foot volumetry, whereby the refill time also acts as the most important parameter[27,28].
These are not discussed further here because they are not used routinely.

Conclusion

Level 3	Plethysmographic investigation can provide information on deep venous insufficiency and on the function of the calf muscle pump. A good, reliable, simple plethysmographic test with which the function of the calf muscle pump can be registered as a number is not widely available. An increase in the venous refill time measured after occlusion of the superficial system may indicate a negative influence of the superficial varicosis on the ambulatory venous pressure. *Ref C* *Van Gerwen 1992[17]; Janssen 1996[18]; Hertsmann 1937[19]; Abramowitz 1979[20];* *Wienert 1982[21]; Blazek 1989[22]; Nickolaides 1987[23]; van Bemmelen 1992[24];* *Bays 1994[25]; Rutgers 1993[26]*

Recommendation 6

Photoplethysmography is not advised for routine investigation because of its low sensitivity and specificity. The remaining plethysmographic methods are not widespread enough at the moment to enable a recommendation.

2.3.2 Other investigation

Systolic ankle pressure index

Scientific basis
It was demonstrated in a number of studies that up to 30% of the total number of patients with a leg ulcer suffer from peripheral arterial vascular disorder. The ulcers hereby may be the result of this peripheral arterial vascular disorder alone or in combination with venous insufficiency. Location of the ulcer may be an indication for peripheral arterial vascular disorder. Therefore, the chances of this occurring in combination with ulceration of the foot are considerably higher than when ulceration is around the ankle[29].
A supplementary investigation of vascular function is required for a correct estimation of the presence and the seriousness of this peripheral arterial vascular disorder as the anamnesis and the physical examination are not enough. The palpation of the ankle/artery at the back of the foot appeared to be insensitive, even carried out by experienced hands, and does not exclude arterial disorder[30-32].
Measuring the systolic ankle pressure in comparison with the systolic arm pressure and calculating the systolic ankle pressure index using a Doppler instrument provides a reliable indicator for the presence of an arterial obstructions. A prerequisite for a valid assessment is that the measurements should be performed in a standardized

manner[33]. An arterial abnormality in an arteriogram is largely excluded (chance >95%) if the systolic ankle pressure index is > 0.8. Measuring the systolic ankle pressure index is not always reliable in the case of patients with diabetes mellitus because compression of the arteries may not be possible (medial sclerosis).

Conclusion

Level 3	An estimated 25% of the patients with a leg ulcer has arterial insufficiency[54]. The palpation of the ankle/artery at the back of the foot is an unreliable test. A systolic ankle pressure index does provide a reliable indication. *C Stoffers 1996[33]*

Recommendation 7

It is recommended that patients with a leg ulcer should be subjected to an additional investigation by measuring systolic ankle pressure index. Further arterial investigation can be undertaken on indication.

Microbial cultures and antibiotics

Scientific basis

Most of the leg ulcers are either contaminated or colonized by bacteria or yeast over a period of time. In larger studies, positive results of cultures were reported in all ulcers[35]. There is a clear relationship between the size of the ulcer, the duration of the ulcer and the age of the patient[34]. Staphylococcus aureus, Streptococci (not group A beta hemolytic) and Pseudomonas aeruginosa were observed in most cultures. The presence of anaerobic bacteria was reported in up to 30% of the cases in one study[36]. Finally, Candida albicans and other fungi were also encountered in 15 to 30% of the ulcers[55].
It was reported in a number of studies that there was no relationship between a positive bacterial culture result and slow wound healing[37-40]. Various authors then also concluded that there was no reason for routine cultures in a venous leg ulcer. A sample for culture is obtained if there are signs of cellulitis or erysipelas, increased pain, an increase in the size of the ulcer, erythema around the wound and a purulent exudate. There is one randomized study in which the effect of antibiotics in the treatment of clinically uninfected ulcers was investigated[41]. However, there was no statistically significant difference between the patients who were treated with antibiotics and those who were not.

Conclusion

Level 3	It is meaningless to routinely obtain a sample from a venous leg ulcer for culture. Culturing and eventual prescription of antibiotics is only indicated if there are signs of an infection of the wound. *B Alinovi 198641*

Recommendation 8

A swab from a venous leg ulcer for culture is warranted only if there are signs of an infection or before surgery on leg ulcers. Oral or intravenous treatment with antibiotics should then also be considered.

Biopsy

Scientific basis

If an ulcer has an atypical appearance or responds inadequately to the therapy, then the possibility of another diagnosis such as a malignancy or a malignant

degeneration should be considered and a skin biopsy should be obtained[42].

Conclusion

Level 3	A biopsy from the edge of the wound may rule out the possibility of a malignancy or a malignant degeneration if the venous leg ulcer responds inadequately to therapy or has an atypical appearance. *C Yang 1996[42]*

Recommendation 9

Taking multiple biopsies should be considered if an ulcer does not respond or responds inadequately to therapy and has an atypical appearance.

Contact allergological investigation

Scientific basis

Eczema cruris in CVI occurs frequently and is often unjustly diagnosed as cellulitis or erysipelas.

A possible contact allergy must always be considered in the case of patients with a long previous history of recurring ulcers. It was shown in various studies that in the case of contact allergies there was generally an allergy to components such as perubalsam and lanoline in wound ointments, to topical antibiotic such as neomycin, wound dressings, bandages[43-49], hydrocolloids and topical anesthetics[47,48,50-52], whereby there was a clear relationship between the duration of the ulcers and the occurrence of contact allergies.

One should always consider the possibility of contact allergy when there are indications of slow wound healing. This often manifests itself in the form of eczema.

Conclusions

Level 3	A contact allergy is often present in patients with persistent or recurrent ulcers. Eczema or a slow healing of the wound may indicate this. *C Wilson 1991[47]; Katsarou-Katsari 1998[48]; Lange 1996[50]; Tosti 1996[51]; Schliz 1996[52]*

Recommendation 10

The recommendation is to carry out a test with a series of allergens that are present in products for treating wounds and wound dressings in addition to the European standard series in all cases of leg eczema in CVI when contact allergy is suspected.

Literature

1. Callam MJ, Ruckley CV, Dale JJ, Harper DR. Hazards of compression treatment of the leg: an estimate from Scottish surgeons. Br Med J (Clin Res Ed) 1987; 295:1382.
2. Classification and grading of chronic venous disease of the lower limb: a consensus statement. Phlebology 1995; 10:42-5.
3. Raju S, Fredericks R. Evaluation of methods for detecting venous reflux. Perspectives in venous insufficiency. Arch Surg 1990; 125:1463-7.
4. Magnusson M, Kalebo P, Lukes P, Sivertsson R, Risberg B. Colour Doppler ultrasound in diagnosing venous insufficiency. A comparison to descending phlebography. Eur J Vasc Endovasc Surg 1995; 9:437-43.

5. McMullin GM, Coleridge Smith PD. An evaluation of Doppler ultrasound and photoplethysmography in the investigation of venous insufficiency. Aust N Z J Surg 1992; 62:270-5.
6. Rautio T, Perala J, Biancari F, Wiik H, Ohtonen P, Haukipuro K, Juvonen T. Accuracy of hand-held Doppler in planning the operation for primary varicose veins. Eur J Vasc Endovasc Surg 2002; 24(5):450-5.
7. Van Bemmelen P, Bedford G, Beach K, Strandness DE. Quantitative segmental evaluation of venous valvular reflux with duplex ultrasound scanning. J Vasc Surg 1989; 10:425-31.
8. Haenen JH, van Langen H, Janssen MC, Wollersheim H, van 't Hof MA, van Asten WN, et al. Venous duplex scanning of the leg: range, variability and reproducibility. Clin Sci (Lond) 1999 Mar; 96(3):271-7.
9. Masuda EM, Kistner RL, Eklof B. Prospective study of duplex scanning for venous reflux: comparison of Valsalva and pneumatic cuff techniques in the reverse Trendelenburg and standing positions. J Vasc Surg 1994; 20 (5):711-20.
10. Baker SR, Burnand KG, Sommerville KM, Thomas ML, Wilson NM, Browse NL. Comparison of venous reflux assessed by duplex scanning and descending phlebography in chronic venous disease. Lancet 1993; 341 (8842):400-3.
11. Masuda EM, Kistner RL. Prospective comparison of duplex scanning and descending venography in the assessment of venous insufficiency. Am J Surg 1992 Sep; 164(3):254-9.
12. Payne SPK, London NJM, Newland DJ, Thrush AJ, Barrie WW, Bell PRF. Ambulatory venous pressure: correlation with skin condition and role in identifying surgically correctable disease. Eur J Vasc Endovasc Surg 1996; 11:195-200.
13. Arnoldi CC. Venous pressures: the function of the venous pump in chronic venous insufficiency. J Cardiovasc Surg 1961; 2:116-127.
14. Kuiper JP. Venous pressure determination (direct method). Dermatologica 1966; 132:206-17.
15. Whitney RJ. The measurement of volume changes in human limbs. J Physiol 1953; 121:1-27.
16. Brakkee A, Vendrik A. Strain gauge plethysmography, theoretical and practical notes on a new design. J Appl Physiol. 1966 Mar; 21(2):701-4.
17. Van Gerwen HJL, Brakkee A, Kuiper JP. Non-invasive measurement of venous muscle pump function in the supine position. Phlebology 1992; 7:146-9.
18. Janssen MCH, Claassen JA, van Asten WN, Wollersheim H, de Rooij MJ, Thien T. Validation of the supine venous pump function test: a new non-invasive tool in the assessment of deep venous insufficiency. Clin Sci 1996;91-483-8.
19. Hertzman AB. Photoelectric plethysmography on the fingers and toes in man. Proc Soc Exp Biol (NY) 1937; 37:529-534.
20. Abramowitz H, Queral LA, Finn WR, Nora PF Jr, Peterson LK, Bergan JJ, et al. The use of photoplethysmography in the assessment of venous insufficiency; a comparison to venous pressure measurements. Surgery 1979; 86:434-41.
21. Wienert V, Blazek V. Eine neue, apparative nichtinvasive Diagnostik der chronisch-venosen Insuffizienz. Phleb u Prokt 1982; 11:110-3.
22. Blazek V, Schmitt HJ, Schulz-Ehrenburg U, Kerner J. Digitale Photoplethysmographie (dPPG) fur die Beinvenendiagnostik - medizinisch-technische Grundlagen. Phleb U Prokt 1989; 18:91-7.
23. Nicolaides AN, Miles C. Photoplethysmography in the assessment of venous insufficiency. J Vasc Surg 1987; 5:405-412.
24. Van Bemmelen PS, van Ramhorst B, Eikelenboom BC.

Photoplethysmography reexamined: lack of correlation with duplex scanning. Surgery 1992; 112:544-8.

25. Bays RA, Healy DA, Atnip RG, Neumyer M, Thiele BL. Validation of airplethysmography, photoplethysmography and duplex ultrasonography in the evaluation of severe venous stasis. J Vasc Surg 1994; 20:721-7.
26. Rutgers PH, Kitslaar PJEM, Ermers EJM. Photoplethysmography in the diagnosis of superficial valvular incompetence. Br J Surg 1993; 80:351-3.
27. Christopoulos D, Nicolaides AN, Szendro G. Venous reflux: quantification and correlation with the severity of venous disease. Br J Surg 1988; 75:352-6.
28. Thulesius O, Norgren L, Gjores JE. Foot volumetry: a new method for objective assessment of oedema and venous function. VASA 1973; 2:325-9.
29. Callam MJ, Harper DR, Dale JJ, Ruckley CV. Chronic ulcer of the leg: clinical history. Br Med J (Clin Res Ed) 1987;294: 1389-91.
30. Magee TR, Stanley PR, al Mufti R, Simpson L, Campbell WB. Should we palpate foot pulses? Ann R Coll Surg Engl 1992; 74:166-8.
31. Brearley S, Shearman CP, Simms MH. Peripheral pulse palpation: an unreliable physical sign. Ann R Coll Surg Engl 1992; 74:169-71.
32. Moffat CJ, Oldroyd MI, Greenhalgh, RM, Franks PJ. Palpating ankle pulses is insufficient in detecting arterial insufficiency in patients with leg ulceration. Phlebology 1994;9:170-2.
33. Stoffers HEJH, Kester ADM, Rinkens PALM, Kitslaar PJEHM, Knottnerus JA. The diagnostic value of the measurement of the ankle-branchial systolic pressure index in primary health care. J Clin Epidemiol 1996; 49:1401-5.
34. Eriksson G, Eklund AE, Kallings LO. The clinical significance of bacterial growth in venous leg ulcers. Scand J Infect Dis. 1984; 16:175-80.
35. Hansson C, Hoborn J, Moller A, Swanbeck G. The microbial flora in venous leg ulcers without clinical signs of infection. Repeated culture using a validated standardised microbiological technique. Acta Derm Venereol 1995; 75(1):24-30.
36. Skene AJ, Smith JM, Dore CJ, Charlett A, Lewis JD. Venous leg ulcers: a prognostic index to predict time to healing. BMJ 1992; 7:1119-21.
37. Margolis DJ, Berlin JA, Strom BL. Which venous leg ulcers will heal with limb compression bandages? Am J Med 2000; 109(1):15-9.
38. Madsen SM, Westh H, Danielsen L, Rosdahl VT. Bacterial colonization and healing of venous leg ulcers. APMIS 1996; 104(12):895-9.
39. Schmidt K, Debus ES, Jessberger ST, Ziegler U, Thiede A. Bacterial population of chronic crural ulcers: is there a difference between the diabetic, the venous, and the arterial ulcer? Vasa 2000; 29(1):62-70.
40. Alinovi A, Bassissi P, Pini M. Systemic administration of antibiotics in the management of venous ulcers. A randomized clinical trial. J Am Acad Dermatol 1986; 15(2 Pt 1):186-91.
41. Yang D. Morrison BD, Vandongen YK, Singh A, Stacey MC. Malignancy in chronic leg ulcers. Med J Aust 1996; 164:718-20.
42. Malten KE, Kuiper JP, van de Staak WJBM. Contact allergic investigations in 100 patients with ulcus cruris. Dermatologica 1973; 147:241-54.
43. Angelini G, Rantuccio F, Meneghini CL. Contact dermatitis in patients with leg ulcers. Contact Dermatitis 1975; 1:81-7.
44. Fraki JE, Peltonen L, Hopsu-Hava VK. Allergy to various components of topical preparations in stasis dermatitis and leg ulcer. Contact Dermatitis 1979; 5:97-100.
45. Kulozik M, Powell SM, Cherry G, Ryan TJ. Contact sensitivity in community-based leg ulcer patients. Clin Exp Dermatol 1988; 13:82-4.
46. Wilson CL, Cameron J, Powell SM, Cherry G, Ryan TJ. High incidence of contact dermatitis in leg ulcer patients - implications for management. Clin Exp Dermatol 1991; 16:250-3.

47. Katsarou-Katsari A, Armenaka M, Katsenis K, Papageorgiou M, Katsambas A, Bareltzides A. Contact allergens in patients with leg ulcers. J Eur Acad Dermatol Venereol 1998;11(1):9-12.
48. Reichert-Penetrat S, Barbaud A, Weber M, Schmutz JL. Leg ulcers. Allergic studies of 359 cases. Ann Dermatol Venereol 1999; 126(2):131-5.
49. Lange IS, Pilz B, Geier J, Frosch PJ. Contact allergy in patients with stasis dermatitis or leg ulcers. Results of the Informational Network of the Departments of Dermatology and the German Contact Allergy Group Dermatosen-in-Beruf-und-Umwelt. 1996; 44:1-22.
50. Tosti A, Vincenzi C, Guerra L, Andrisano E. Contact dermatitis from fatty alcohols. Contact Dermatitis 1996; 35(5):287-9.
51. Schliz M, Rauterberg A, Weiss J. Allergic contact dermatitis from hydrocolloid dressings. Contact Dermatitis 1996; 34(2):146-7.
52. Scriven JM, Taylor LE, Wood AJ, Bell PR, Naylor AR, London NJ. A prospective randomised trial of four-layer versus short stretch compression bandages for the treatment of venous leg ulcers. Ann R Coll Surg Engl 1998; 80(3):215-20.
53. Eklof B, Rutherford RB, Bergan JJ, Carpentier PH, Gloviczki P, Kistner RL, Meissner MH, Moneta GL, Myers K, Padberg FT, Perrin M, Ruckley CV, Smith PC, Wakefield TW. Revision of the CEAP classification for chronic venous disorders: Consensus statement. J Vasc Surg 2004; 40: 1248-52.
54. Ramelet AA. Ulcere de jambe - Bacteriologie. Phlebologie 1999; 52: 393-397.
55. Nelson EA, Bradley MD. Dressings and topical agents for arterial leg ulcers. Cochrane Database of Systematic Reviews 2007, Issue 1.
56. Hansson C, Jekler J, Swanbeck G. Candida albicans infections in leg ulcers and surrounding skin after the use of ointment impregnated stockings. Acta Derm Venereol. 1985;65(5):424-7.

CHAPTER 3. COMPRESSION THERAPY

Introduction

Compression therapy may be carried out in different ways. On the one hand, with bandages (without stretch, with a short stretch or a long stretch) and on the other hand, with medical elastic compression hosiery (MECH). Finally, the compression may also be pneumatic and provided by a pneumatic pump, but this is not further commented on in this guideline.

Some still make a distinction for the medium stretch bandages, but these are not encountered in medical literature. In particular, bandages may also have an adhesive layer, in which case the bandage can only be used once. Generally, the bandages do not stretch in the breadth, but this is not mentioned in the encountered literature. Several layers of bandages may be placed over each other to increase the compression. Generally, bandages of the same quality are involved. A system popular in England uses a combination of short stretch and long stretch compression known as four-layer-bandage.

MECH, which are medically approved, always have a decreasing compression gradient from distal to proximal. They are divided into compression classes, whereby the division is determined by the compression of the MECH on the skin above the malleoli. The Comite Europeen de Normalisation (CEN) (ENV 12718) has set a standard for MECH in Europe. The compression classes are (based on the B-size): pressure class A (light) 10-14 mm Hg (13-19 hPa), class I (mild) 15-21 mm Hg (20-28 hPa), class II (moderate) 23-32 mm Hg (31-43 hPa), class III (strong) 34-46 mm Hg (45-61 hPa), class IV (extra strong) >49 mm Hg (>65 hPa).[1] One should realize that an anti-thrombosis stocking is of class I without pressure gradient. These

stockings are meant for bed-ridden individuals and remain beyond the scope of this discussion. Various options for compression are compared in this chapter.

3.1 Compression versus no compression

Scientific basis

Compression systems for leg ulcers have been compared in various systematic reviews. It appeared that the same articles were constantly included in some reviews. The conclusion endorsed by many is that healing is faster with the use of compression than without[2-11]. There are no studies in which the reverse was reported. Compression therapy is also consistently recommended in international guidelines[3,5-10]. There are reviews from which one can deduce that there is indirect evidence that compression leads to faster healing, although few good studies are available in which compression was compared with no compression[13,14].

Conclusion

Level 1	Compression therapy is an effective treatment in uncomplicated venous ulcers. *A1* *Fletcher 1997[2]; Cullum 2001[3]; SIGN 1998[5];*

Recommendation 11

Compression therapy is the treatment of first choice in an uncomplicated venous leg ulcer.

3.2 Comparison of different types of compression bandages

Scientific basis

A lot of studies in which various types of bandages were used are compared in different reviews. A generally accepted conclusion is that a high compression is more effective than a low compression in the healing of a venous leg ulcer[2,4,7,9,10].
Venous reflux can be reduced more effectively with a short stretch bandage than with an elastic one[24]. A short stretch compression and Unna´s boot supports the pump function of the calf muscles better than a long stretch compression[29,30].
Generally, more layers of a bandage are applied on top of each other because a single layer bandage provides less compression than a multiple layer bandage[2].
In comparative studies on different types of bandages, multiple layers of different elastic bandages were described to be more effective than a short stretch bandage[2].
A comparison of short stretch bandages with a four-layer-bandage (combination of four different layers) showed that after 16 weeks there was healing in 62% of those treated with a four-layer bandage and in 73% of those treated with a short stretch bandage (difference not significant)[15]. It made no difference which bandage was used[2-4,6-9,17], provided it was correctly applied[2-6,8,10].
Small ulcers of short duration may also successfully be treated with compression stockings providing a pressure of =40 mm Hg[7]. The four-layer-bandage is very popular in the United Kingdom because the care for a patient with a venous leg ulcer is almost exclusively provided by nurses. Little specific training or experience is required in the application of a four-layer-bandage[5,6,15,16,17].

Conclusions

Level 1	There is no evidence that a particular type of bandage is the best.A bandage must be properly applied, and that requires training. *A1* *Fletcher 1997[2]; Culum 2001[3]; Kurz 1999[4]; SIGN 1998[5]; Agus 2001a[6];*

	Vin 20031[7]

Level 1	High-pressure compression is more effective than low-pressure compression.Multiple layers of a bandage are required to provide adequate compression. *A1* *Fletcher 1997*[2]*; Kurz 1999*[4]*; Agus 2001b*[7]*; Vin 2003*[17]

Other considerations
Simple, but more expensive bandaging techniques are available for those with inadequate bandaging experience. High pressure elastic bandages are strictly contraindicated in patients with arterial occlusive disease. The pressure depends on the person who is carrying out the compression and on the elasticity. Long stretch bandages provide a more constant high pressure than short strech bandages, leading to a greater risk for people with arterial occlusive disease.

Recommendation 12

A properly applied high compression bandage should be used in an uncomplicated venous leg ulcer. A four-layer-bandage is worth considering if the bandaging staff is inexperienced in the application of high pressure bandages.

Compression with medical elastical compression hosiery (MECH)

Scientific basis
It was established in systemic reviews that MECH exerting a pressure that exceeded or was equal to 35 mm Hg may also be used in the treatment of venous leg ulcers[4,7]. The compliance was 70% and few side effects were reported[4].
Special MECHS for the treatment of leg ulcers have been available on the market for a number of years. In two randomized controlled trials results that were even better or at least similar to those with classical compression therapy were reported [19,20].

Conclusion

Level 3	MECH exerting a pressure of =35 mm Hg (45 hPa) may also be used in the treatment of an uncomplicated venous leg ulcer. Special so-called leg ulcer MECH are at least as effective as CT. *B* *Mayberry 1991*[20]*; Erikson 1995*[21] *B* *Junger*[27]*; Junger*[28]

Other considerations
Recently, bandage stockings for treating venous leg ulcers have been introduced on the market. At present there are insufficient studies to allow any comment on their effect.

Recommendation 13

Reduction of edema may be brought about cheaply and generally quickly when short stretch bandages are correctly applied. Well-chosen and correctly measured MECH may be switched to when the size and level of exudation of the ulcer allow it.

Intermittent pneumatic compression
Intermittent pneumatic compression pumps may be a useful adjunct in ulcer healing. Such supplementary compression may be especially useful for patients with restricted walking ability and those with an arterial component in their ulcer[25,26].

Literature

1. Hulpmiddelen Kompas Therapeutisch Elastische kousen. Amstelveen: college voor Zorgverzekeringen; 2002.
2. Fletcher A, Cullum N, Sheldon TA. A systematic review of compression treatment for venous leg ulcers. BMJ 1997; 315(7108):576-80.
3. Cullum N, Nelson EA, Fletcher AW, Sheldon TA. Compression for venous leg ulcers (Cochrane review) In: The Cochrane Library, issue 4: 2001, Oxford.
4. Kurz X, Kahn SR, Abenhaim L, Clement D, Norgrens L, Baccaglini U, Berard A, Cooke JP, Cornu-Thenard A et al. Chronic venous disorders of the leg: epidemiology, outcomes, diagnosis and management. Consensus statement. Int Angiol 1999; 18: 83-102.
5. Scottish Intercollegiate Guidelines Network (SIGN). The care of patients with chronic leg ulcer; a national clinic guideline. 1998;1-26.
6. Agus GB, Allegra C, Arpaia G, Botta G, Cataldi A, Gasbarro V, et al. Guidelines on compression therapy. Acta Phlebologica 2001a; suppl. 1:1-24.
7. Partsch H, Horakova MA. Compression stockings in treatment of lower leg venous ulcer. Wien Med Wochenschr. 1994; 144: 242-9.
8. Agus GB, Allegra C, Arpaia G, Botta G, Cataldi A, Gasbarro V, et al. Guidelines for the diagnosis and treatment of diseases of the veins and lymphatic vessels: Evidence-based report by the Italian College of Phlebology. Int angiol 2001b;20 Suppl 2:6-27.
9. Coleridge Smith PD (ed.). The management of chronic venous disorders of the leg: an evidence-based report of an international task force. Phlebology 1999;14 Suppl 1: 1-126.
10. New Zealand Guidelines Group, the Royal New Zealand College of General Practitioners. Care of people with chronic leg ulcers. An evidence based guideline. 1999;1-50.
11. RCN Institute, Centre for Evidence Based Nursing, University of York and the school of Nursing, Midwifery and Health Visiting, University of Manchester. Clinical Practice Guidelines. The management of patients with venous leg ulcers. Oxford: RCN; 1998.
12. Stacey MC, Hoskin SE, Van dongen Y, Pearce C. Efficacy and cost effectiveness of compression bandaging in venous ulcer healing. Int angiol 2001; 20: suppl 1: 338.
13. Palfreyman SJ, Lochiel R, Michaels JA. A systematic review of compression therapy for venous leg ulcers. Vasc Med 1998;3(4):301-13.
14. Kikta MJ, Schuler JJ, Meyer JP, Durham JR, Edrup-Jorgensen J, Schwarcz TH, et al. A prospective, randomized trial of Unna's boot versus hydroactive dressing in the treatment of venous stasis ulcers. J Vasc Surg 1988;7:478-86.
15. Partsch H, Damstra RJ, Tazelaar DJ, Schuller-Petrovic S, Velders AJ, de Rooij MJ, et al. Multicentre, randomised controlled trial of four-layer bandaging versus short-stretch bandaging in the treatment of venous leg ulcers. Vasa 2001;30(2):108-13.
16. Scriven JM, Taylor LE, Wood AJ, Bell PR, Naylor AR, London NJ. A prospective randomised trial of four-layer versus short stretch compression bandages for the treatment of venous leg ulcers. Ann R Coll Surg Engl 1998;80(3):215-20.
17. Vin F, Benigni JP. Conference internationale de consensus sur la compression. Plebologie 2003; 56:315-67.
18. Castineira F, Fisher H, Coleman D, Grace PA, Burke P. The Limerick Leg-Ulcer Project: early results. Ir J Med Sci 1999;168(1):17-20.
19. Margolis DJ, Berlin JA, Strom BL. Which venous leg ulcers will heal with limb compression bandages? Am J Med 2000;109(1):15-9.
20. Mayberry JC, Moneta GL, de Frang RD, Porter JM. The influence of elastic compression stockings on deep venous hemodynamics. J Vasc Surg 1991;13:91-100.

21. Erikson CA, Lanza DL, Karp DL et al. Healing of venous ulcers in an ambulatory care program: the roles of chronic venous insufficiency and patient compliance. J Vasc Sug 1995;22:629-36.
22. Partsch H, Clark M, Bassez S, Benigni JP, Becker F, Blazek V, Caprini J, Cornu-Thenard A, Hafner J, Flour M, Junger M, Moffatt C, Neumann M. Measurement of lower leg compression in vivo: recommendations for the performance of measurements of interface pressure and stiffness: consensus statement. Dermatol Surg. 2006; 32: 229-38.
23. Junger M. Vascular sport therapy in chronic venous insufficiency and peripheral arterial occlusive disease. Hautarzt. 1994; 45: 257-9.
24. Partsch H, Menzinger G, Mostbeck A, Inelastic leg compression is more effective to reduce deep venous refluxes than elastic bandages. Dermatol Surg 1999; 25: 695-700.
25. Kumar S, Samraj K, Nirujogi V, Budnik J, Walker MA. Intermittent pneumatic compression as an adjuvant therapy in venous ulcer disease. J Tissue Viability. 2002 Apr;12:42-4.
26. Mani R, Vowden K, Nelson EA. Intermittent pneumatic compression for treating venous leg ulcers (Cochrane Review). In: The Cochrane Library, Issue 3, 2004. Chichester, UK: John Wiley & Sons, Ltd.
27. Junger M, Partsch H, Ramelet A.-A, Zuccarelli F. Efficacy of a ready-made tubular compression device versus short-stretch compression bandages in the treatment of venous leg ulcers. Wounds 2004; 16: 313-320.
28. Junger M, Wollina U, Kohnen R, Rabe E. Efficacy and tolerability of an ulcer compression stocking for therapy of chronic venous ulcer compared with a below-knee compression bandage: results from a prospective, randomized, multicenter trial. Curr Med Res Opin. 2004; 20: 1613-23.
29. Partsch H.The static stiffness index: a simple method to assess the elastic property of compression material in vivo. Dermatol Surg. 2005 Jun;31 (6):625-30.
30. Polignano R, Bonadeo P, Gasbarro S, Allegra C. A randomised controlled study of four-layer compression versus Unna's Boot for venous ulcers. J Wound Care. 2004 Jan;13(1):21-4.

CHAPTER 4. TREATMENT OF WOUNDS

Introduction

One rapidly comes to the conclusion that very little is known about the effect of the treatment during the various stages of the wound healing when one searches on the treatment of wounds in the databanks and in the textbooks. Nonetheless, we are continuously seeing more results of experimental animal studies into the role of oxygen radicals, cytokines, growth factors and matrix-metalloproteases. One of the problems in developing new wound products is that there is no ideal animal model for a chronic wound. Thus, increased animal wound healing results cannot be transferred to the human situation.

The cause of the poor healing of venous ulcers is sought in local abnormalities in and around the ulcer, shortage of oxygen, accumulation of granulocytes and T lymphocytes and a disturbed balance of cytokines and growth factors. Treatment of wounds, in an adverse sense, is subordinate to treating the primary disorder, namely, the increased venous pressure.

The working group did not use the scheme by the Woundcare Consultant Society (WCS) for the description of the treatment of wounds.

Recommendation 14

The working group is of the opinion that the level of cleansing and exudation are the most important parameters for further treatment policy in the case of venous leg ulcers.

4.1 Cleansing

Scientific basis

Little is known in medical literature on the effects of different cleansing methods. One study on pressure ulcers reported a significant improvement of the ulcers with a spray containing Aloe vera, silver chloride an decyl glucoside (vulnoper) compared with sulike as control. As mentioned earlier (see chapter on diagnostics), the chronic wounds are colonized with bacteria, for which necrotic tissue encounter is a good nutrient medium. As a start in the treatment, removal of necrosis seems essential, considering that the removal also leads to stimulation of the formation of granular tissue and a lowering of the risk of infection[1,2].

Conclusion

Level 3	Necrotomy reduces the level of contamination and speeds up granulation.CT. *C* *Falabella 1998a*[1]

Under cleansing, we understand the removal of necrosis, fibrin batter or other wound debris.
Necrotic tissue may be surgically removed or treated with an enzymatic wound cleanser. The wound will cleanse itself via autolysis if none of these methods is chosen. An experienced physician should perform the surgical intervention in order to avoid damage to healthy tissue.
There are two commercial products available for an enzymatic treatment. These are fibrinolysin/pancreasdornase (Elase®) and collagenase (Novuxol®). It appeared from animal experimental studies by Mekkes and from investigations by Falabella that there were no indications of any positive effect on the removal of necrosis[3,4]. In one review, only collagenase was reported to be possibly effective[5].
Many manufacturers claimed that the use of modern wound dressings had a positive effect on the speed of autolysis. In an investigation by Bradley et al it was reported that there was no reason for using any of these products for this purpose[2].
A fibrin batter is often left behind after most of the necrosis has been removed. Antiseptics such as povidone-iodine, chlorhexidine, acetic acid or sodium hypochlorite/paraffin are then often chosen as the treatment of preference. In a systematic review of all the studies in this area it appeared that no conclusions could be drawn to justify the use of these, in principle, cytotoxic agents[6]. The users purely base the frequent use of sodium hypochlorite in the Netherlands on individual experience and verbal advertising.
Cleansing with normal tap water has the same result as cleansing with an isotonic sodium solution[7].
There are no known studies on the value of baths (soda or washing-powder). The moisture-absorbing effect of detergents will have an adverse effect on the wound and the surrounding area.
For the removal of necrotic tissue, sharp debridement is the treatment of choice[27]. This debridement can be performed using a variety of methods ranging from scalpel and curette, to more advanced methods such as high pressure hydrojet and ultrasound systems. Recently, several low pressure hydrojet systems have become available, which are highly suitable for rinsing a wound with any chosen solution, but are not as effective as high pressure hydrojet systems for the removal of debris.
Treatment with maggots has been known since the First World War. Maggots are excellent necrophages. Affectivity, but not in relation to venous leg ulcers, was described in case reports.

Conclusions

Level 3	Surgical necrotomy is an efficient and preferred treatment. *C* *Falanga 2001*[8] *A2* *Williams 2005*[27]

Level 3	There are indications that collagenase is the only enzymatic agent that speeds up debridement. *B* *Bergemann 1999*[4]

Level 3	It has not been demonstrated that wound dressings speed up autolysis. *C* *Bradley 1999*[2]

Level 1	Topical antiseptics are ineffective in cleansing ulcers and are, in principle, cytotoxic. *A1* *O'Meara 2001*[6]

Level 3	Tap water cleanses as good as physiological saline. *B* *Angeras 1992*[7]

Recommendation 15

The working group is of the opinion that the following aspects are important when cleansing an ulcer:

- Begin with a surgical necrotomy if possible.
- Collagenase is the only agent for enzymatic treatment.
- Use no topical antiseptics.
- Cleanse wounds with tap water.

4.2 Wound dressings

Scientific basis

Publications, among others by Winter, in which the advantages of wet treatment of wounds in comparison with "wet-gauzes" were demonstrated, already appeared towards the beginning of the1960s. It led to faster healing. The frequently used treatment with gauzes had many disadvantages such as bleeding and pain upon removal and granular tissue damage when the dressings were changed. The necessary frequent changing also led to a disturbed healing of the wound. Therefore, products that enable the creation of a moist wound environment were introduced. An added advantage is that these products stick less to the wound bed, something that happens regularly with "wet-gauzes".

Hydro gels, hydrocolloids, alginates, foam bandages and transparent foils are available for the treatment of leg ulcers. The choice of the product also depends on the level of exudation from the wound considering that each of the products has a different resorption capacity. Hydro gels, hydrocolloids and transparent foils without other applications should be used either for non-exudating wounds or wounds that exudate a little, taking into account the fact that the chance of maceration of the edges of the wound is then high. Alginates are used when exudation is moderate to high. Foam bandages may be used in all types of exudation. No clear difference in the effectiveness, also not of traditional bandages or modern bandages was reported

in medical literature. The logistical aspect favors the more modern means. An extensive review of 31 papers was not conclusive[29].
The influence of antiseptic agents was reported by Kramer et al (2004)[25].

Conclusion

Level 4	There are indications that modern wound dressings are better than the traditional gauzes in the healing of wounds. *D Bradley 1999*[9]

Other considerations
It appeared in practice that modern wound dressings offered advantages compared with traditional gauzes (moist wound environment, less pain and damage to the wound bed when dressings are changed and a lower frequency of changing the dressings). Patients prefer this. Furthermore modern wound dressings work well in combination with compression bandages and elastic hosiery.

Recommendation 16

The working group advises modern wound dressings for achieving a moist wound environment also because the dressings do not need to be changed as frequently. The choice of a particular product depends mainly on the level of exudation.

4.3 Antibacterial agents

Scientific basis
Although ulcers as a rule are contaminated, it is useless to routinely obtain samples for culture and/or to treat them systemically with antibiotics (see also chapter on diagnostics). The use of antibiotics may lead to resistance. In a randomized study by Alinovi et al, it was observed that, when using systemic antibiotics, there was no statistically significant difference between user/non-user in healing and that there were no changes in the flora[10]. A sample from the wound for culture and an adequate systemic treatment based on the sensitivity spectrum is meaningful only when there are clinical indications of an extensive infection (cellulitis, erysipelas, osteomyelitis).
The topical effect of silver sulfadiazine was also looked at in various studies included in the systematic review by O'Meara et al[6]. Silver sulfadiazine was observed to be effective when compared to a placebo. One should take into account that prolonged use in experimental animals led to an accumulation of silver/paraffin as a cuff around the blood vessels. The extent to which this phenomenon, which is encountered in burns, also plays a role in venous leg ulcer remains unknown, but must be included in the further treatment if wound healing stagnates. Recently, many wound dressings containing a low concentration of silver for anti-bacterial effect have appeared on the market. To date, there is no evidence that wound dressings containing silver lead to faster wound healing[26].
Fusidic acid is regularly prescribed as first line care. Unfortunately, no basis is found for this in medical literature. Metronidazole is paticularly used on oncological ulcers against the odor produced by the anaerobes. However, there is no indication that the use of metronidazole can lead to resistance[11].
The use of topical antibiotics is not advised because of the development of resistance and contact allergy (see there). This has been demonstrated for sofra-, genta- and neomycin.
Acetic acid has been used in pseudomonas-infected ulcers for a long time now. It is hereby assumed that a pseudomonas infection has an adverse effect on wound healing. An expert team of dermatologists shares this view, but evidence for this statement is lacking.
From this point of view, eradication of the pseudomonas contamination should speed up wound healing. This may be achieved practically with antibiotics effective against

pseudomonas. However, only one oral antibiotic family is available against pseudomonas. Resistance generally develops after several days of this monotherapy. Therefore, attempts have been made to develop other methods effective against pseudomonas infection. Acetic acid has anti-pseudomonas effect and is therefore used extensively in practice. Patients experienced painful treatment as a disadvantage. Moreover, the treatment has to be repeated several times and the effect of acetic acid on wound healing alone has not been investigated.
In practice, a 0.5%-1% acetic acid solution appeared to be effective. The odor produced by the bacteria generally disappeared after 3 days, which may be regarded as proof of the effectiveness.

Conclusions

Level 3	Systemic treatment with antibiotics appeared to be meaningless in venous leg ulcers without signs of an active infection. *B* *Alinovi 1986*[10]

Level 1	In general, there is no evidence that silver-containing wound dressings are more effective than those without silver. *A1* *Bergin SM*[26]

Level 3	Topical antibiotics have no place in the treatment. *B* *Kay 2000*[11]

Level 4	Topical antiseptics are ineffective in cleansing ulcers and are, in principle, cytotoxic. Topical 0.5%-1% acetic acid solution may be used to treat wounds contaminated with pseudomonas. However, a scientific basis is lacking for this.

Recommendation 17

Silver sulfadiazine/paraffin is the only eligible antimicrobial agent for topical use.

4.4 Skin replacement products

Scientific basis
Tissue-engineered skin graft products appear to be a highly promising treatment. A good and rapid healing must be achieved if this type of product adequately covers the ulcer after extensive preparation of the wound bed. In medical literature, there is only one randomized study in 120 patients by Falanga et al who reported that treatment with a skin graft was more effective after 6 months and 1 year in ulcers that had persisted for longer than a year[12].

Conclusion

Level 3	There are indications that tissue-engineered skin graft products may have a future in the treatment of venous leg ulcers. *B* *Falanga 1998*[12]

Recommendation 18

Tissue-engineered skin grafts have a possible place in the future for treating venous ulcers.

Conventional wound dressings sometimes do not offer a satisfactory solution for treating leg ulcers. An alternative is treatment with transplanted skin (cells). There is limited indication for this here, but this is scientifically supported, with some difficulty[13].

There are various transplantation alternatives. One can use the skin of the patient (split-skin transplantation or biopsy/reverdin´s plasty), culturing the cells from the skin of the patient (autograft) or one can use tissue-engineered skin of donor cells (allograft).
There are several randomized studies in which transplantation on venous ulcers was investigated[12,14-19]. It can generally be stated that these studies were of moderate quality and did not always adequately prove the added value of transplantation.
Poskitt and Warburg investigated split-skin transplantation[14,15]. The additional value of split-skin could not be proven because of the small number of patients that was investigated.
It has not been proven that cultured keratinocytes (allografts) are a better choice than conventional wound dressings. There was no difference between split-skin transplantation and allograft transplantation[19].
In a retrospective study in which ulcers were treated with biopsy transplantation there was healing in 38% of the patients after six months .[20] A recurrence was observed in 27% of the patients.
Schmeller described a special technique that involved excision of the ulcer area and all the surrounding dermato-et liposclerosis up to the healthy tissue, followed by a split-skin graft[21]. Of the 59 patients (76 ulcers), 79% healed in 3 months.
Unfortunately, others did not report on this technique and no RCT is available.
The value of transplantation has not been proven.

Conclusion

Level 1	The additional value of (various sorts) of transplantation in the treatment of venous ulcers has not been proven. It is possible that transplantation may speed up the healing of ulcers. Good randomized studies are necessary to prove this. *A1 Jones 2002*[13]

Other considerations
Nothing has been reported on the cost-effectiveness of the various ways of transplantation in relation to the conventional treatment. It can generally be assumed that this treatment will be financially unattractive if the period of healing is not evidently shorter.

Recommendation 19

The working group is of the opinion that skin grafting may be a useful treatment on indication.

Negative pressure treatment
Scientific basis
There are still many wounds with very poor tendency to heal despite the arrival of the modern wound dressings. Negative pressure treatment (vacuum assisted closure - VAC) is used to stimulate wound healing through constant suction of wound fluid, leading to a reduction in the level of contamination, thus speeding up angiogenesis and granulation. It appeared in two small trials that VAC was superior to treatment with physiological saline-drenched gauzes[22]. It has hard to formulate useful advice because of the small numbers and methodological limitations. More randomized

investigation is necessary before any scientifically based advice can be given[28].

Conclusion

Level 3	Two trials aimed at investigating whether negative pressure treatment leads to faster wound healing were of insufficient power to enable this conclusion. *B Evans 2001*[22]

4.7 Treatment of local pain

Scientific basis

Venous ulcers can be painful. Most of the modern wound dressings claim to reduce pain.

The pain is caused by the exposed nerve endings. A moist wound environment prevents dehydration and thereby reduces pain. In two trials, one with a hydrocolloid and one with a foam dressing, there was less pain when the dressings were changed and during application than with other non-adhesive dressings. Three studies in which the use of Emla® clearly reduced the feeling of pain during the debridement in venous ulcers were reported[24]. Whether this slows down wound healing is unclear.

Conclusion

Level 3	There are indications that pain in combined ulcers is reduced by the use of either a hydrocolloid or a foam dressing. Use of Emla cream reduces the pain caused by necrotomy. *C Briggs 2001*[24]

Literature

1. Falabella A. Debridement of wounds. Wounds 1998;10(suppl C):1-8.
2. Bradley M, Cullem N, Sheldon T. The debridement of chronic wounds: A systemic review. Health Technology Assessment 1999; 3(17 Pt 1).
3. Mekkes JR. Debridement of venous leg ulcers. Ph.D. thesis, University of Amsterdam; 1998.
4. Falabella AF, Carson P, Eaglstein WH, Falanga V. The safety and efficacy of a proteolytic ointment in the treatment of chronic ulcers of the lower extremity. J Am Acad Dermatol.1998; 737-70.
5. Bergemann R, Lauterbach KW, Vanscheidt W, Neander KD, Engst R. Economic evaluation of the treatment of chronic wounds: hydroactive wound dressings in combination with enzymatic ointment versus gauze dressings in patients with pressure ulcer and venous leg ulcer in Germany. Pharmacoeconomics. 1999 Oct; 16(4):367-77.
6. O'Meara SM, Cullum NA, Majid M and Sheldon TA. Systemic review of antimicrobial agents used for chronic wounds. Br J Surg 2001; 88:4-21.
7. Angeras MH, Bradberg A, Falk A, Seeman T. Comparison between sterile saline and tapwater for cleansing of acute soft tissue wounds. Eur J Surg 1992; 158:347-50.
8. Falanga V (ed). Cutaneous wound healing. London: Martin Dunitz; 2001.
9. Bradley M, Cullem N, Nelson EA, Petticrew M, Sheldon T, Togerson D. Systemic reviews of wound care management: Dressings and topical agents used in the healing of chronic wounds. Health Technology Assessment 1999; 3(17 Pt 2).
10. Alinovi A, Bassissi P, Pini M. Systemic administration of antibiotics in the

management of venous ulcers. J Am Acad Dermatol. 1986; 15(2):186-91.

11. Kaye ET. Topical antibacterial agents. Infect Dis Clin North Am 2000; 14 (2):321-39.
12. Falanga V, Margolis D, Alvarerez O, Auletta M, Maggiacomo F, Altman M, et al. Rapid healing of venous ulcers and lack of clinical rejection with an allogenic cultured human skin equivalent. Arch Dermatol 1998; 134:293-300.
13. Jones JE, Nelson EA. Skin grafting for venous leg ulcers (Cochrane Review). In: The Cochrane Library, Issue 3, 2000. Oxford: update software.
14. Poskitt K, James AM, Lloyd-Davies E, Walton J, McCollum C: Pinch skin grafting or porcine dermis in venous leg ulcers: a randomised clinical trial. Br Med J 1987; 294:674-6.
15. Warburg F, Danielsen L, Madsen Set al. Vein surgery with or without skin grafting versus conservative treatment for leg ulcers. Acta Dermato Ven 1994; 74:307-9.
16. Duhra P, Blight A, Mountford E et al. A randomised controlled trial of cultured keratinocyte allografts for chronic venous ulcers. J Dermatol Treatment 1992; 3:189-191.
17. Lindgren C, Marcusson J, Toftgard R. Treatment of venous leg ulcers with cryopreserved cultured allogenic keratinocytes: a prospective open controlled study. Br J Derm 1998; 24:77-82.
18. Teepe R, Roseeuw D, Hermans J, Koebrugge EJ, Altena T, De Coninck A, et al. Randomized trial comparing cryopreserved cultured epidermal allograft with hydrocolloid dressings in healing chronic venous ulcers. J Am Acad Dermatol 1993; 29:982-9.
19. Mol M, Nanninga B, Eendenburg J, Westerhof J, Mekkes J, van Ginkel C. Grafting of venous leg ulcers. J Am Acad Dermatol 1991; 24:77-82.
20. Christiansen J, Ek L, Tegner E. Pinch grafting of leg ulcers. Acta Derm Venereol (Stockh) 1997; 77:471-3.
21. Schmeller W, Gaber Y, Gehl HB. Shave therapy is a simple, effective treatment for persistent venous leg ulcers. J Am Acad Dermatol 1998; 39:232-8.
22. Evans D, Land L. Topical negative pressure for treating chronic wounds (Cochrane Review) The Cochrane Library, Issue 4, 2001. Oxford: Update Software.
23. Declair V. Ostomy/Wound management. 1999 april 45(4):64-79.
24. Briggs M, Nelson EA. Topical agents of dressings for pain in venous leg ulcers. Cochrane review. The Cochrane Library, Issue 4, 2001. Oxford: Update software.
25. Kramer A, Roth B, Muller G, Rudolph P, Klocker N. Influence of the antiseptic agents polyhexanide and octenidine on FL cells and on healing of experimental superficial aseptic wounds in piglets. A double-blind, randomised, stratified, controlled, parallel-group study. Skin Pharmacol Physiol. 2004; 17: 141-6.
26. Bergin SM, Wraight P. Silver based wound dressings and topical agents for treating diabetic foot ulcers. Cochrane Database Syst Rev. 2006; 25: 1. Cochrane Database Syst Rev. 2006 Jan 25;(1).
27. Williams D, Enoch S, Miller D, Harris K, Price P, Harding KG. Effect of sharp debridement using curette on recalcitrant nonhealing venous leg ulcers: A concurrently controlled prospective cohort study. Wound Rep Reg 2005; 13: 131-137.
28. Shirakawa M, Isseroff RR. Topical negative pressure devices: use for enhancement of healing chronic wounds. Arch Dermatol. 2005; 141: 1449-53.
29. Bouza C, Munoz A, Amate JM. Efficacy of modern dressings in the treatment of leg ulcers: A systematic review. Wound Repair Regen. 2005; 13(3): 218-

29.

CHAPTER 5. INVASIVE TREATMENT

Introduction

The surgical treatment of venous leg ulcers has been extensively described in medical literature and used worldwide. This treatment involves surgical intervention of the superficial venous system, the deep venous system, or the perforating venous system; a combined treatment of these three systems is also possible.
The precise pathogenesis and the role played by these three venous systems in the development of a venous leg ulcer are highly controversial. Studies of this treatment are mainly uncontrolled and are incomparable with each other. In many series, different treatments of non-uniform patient populations are presented.
An attempt has also been made to reach a consensus on the effective contribution of surgery to the healing of venous leg ulcers in the countries surrounding the Netherlands. As stated in the Scottish guidelines, there is no proof whether surgery should be chosen for treatment in case of chronic venous ulcer (an active ulcer; C6), or as secondary prevention after healing of the ulcer (C5) (CEAP-classification).
There is consensus that superficial venous surgery may effectively contribute to the healing of the ulcer in case of a sufficient deep venous system[1]. Later on, surgery may contribute to the quality of life for patients with varicose veins[29].
There are two randomized, controlled clinical trials indicating the role of surgery in the treatment of venous leg ulcers, compared to conservative therapy[36,37].

5.1 Superficial venous system

Scientific basis

Superficial venous insufficiency is present in about 80% of venous ulcer patients, and half of them are associated with deep incompetence. There aren't any good, randomized studies on the role of isolated insufficiency of the superficial system and it surgical treatment. Good results were observed in a number of studies in which some or all of the patients received ambulatory compression therapy after the superficial system had been cleaned up surgically, which made its contribution difficult to assess.
In a prospective cohort study, Barwell et al reported that surgery of the superficial system in isolated insufficiency led to a lower recurrence than if no surgery had been performed.[2]
In a prospective, non-randomized study, Bello et al reported that the surgical treatment of this isolated insufficiency led to healing in most patients without additional ambulatory compression therapy[3]. However, Scriven et al also reported the same conclusion, but in a smaller series[4].
Surgical treatment of the superficial venous system consists of a crossectomy of the great saphenous vein (GSV) by stripping distally till within a handbreadth from the knee and/or a crossectomy of the small saphenous vein (SSV). Stripping of SSV is not reported in any publication.

5.2 New treatments for imcompetent superficial venous system

As of recently, there are new minimal invasive techniques such as the VNUS-procedure, endovascular lasertherapy and echo-guided sclero-compression therapy (foam), which can replace classical surgery for treating varices. The first results are very promising[30,31,32,33,34,35,36,37].

Conclusion

Level 2	Surgical treatment of isolated insufficiency of the superficial system in a venous leg ulcer may promote healing, and reduce the recurrence rate. *B* *Scriven 1998[4]; De Palma 1996[5]* *C* *Barwell 2000[2]; Bello 1999[3]; Padberg 1996[6]; Clement 1999[7]*

Recommendation 20

The working group is of the opinion that a combination of surgical treatment and ambulatory compression therapy is preferred in the case of an isolated insufficiency of the superficial system in a venous leg ulcer.

5.3 Deep venous system

Scientific basis

One can use different techniques such as valve repair, valve transposition or valve transplantation for the reconstruction of venous valve[8]. Recently, Raju et al reported a variation of an external valve repair technique (transcommissural valvuloplasty), whereby they concluded that this was a safe procedure with a low morbidity[9]. The same group also reported a study in which cryo-preserved venous valve allografts were used to treat deep venous insufficiency[10]. There are no good, randomized comparative studies with a prolonged follow-up period on the effect of venous valve reconstruction in the treatment of deep venous insufficiency. There has not yet been any proven effect on the healing of venous leg ulcers.

Conclusion

Level 3	From a pathophysiological point of view, reconstruction of venous valves would be the ideal solution in the case of deep venous insufficiency, but up till now all these techniques have only produced a valve reconstruction of limited duration, while they require extensive surgery. New developments aimed at replacing the deep insufficient venous valve with a percutaneously inserted biological or an artificial valve are still experimental. The effect on the healing of a venous leg ulcer has not been proven. *B* *Dalsing 1999[10]* *C* *Masuda 1994[8]; Raju 2000[9]*

5.4 Perforator (venous) system

Scientific basis

The role of the perforating veins (venae perforantes) in the pathogenesis of venous leg ulcers is not yet known and remains controversial. Isolated insufficiency of the perforatory system is seldom encountered in patients with a venous ulcer.
Various published series showed that surgery of incompetent perforators yielded good results in the treatment of venous leg ulcers[11-21].
In a recent (finished after closing literature search) Dutch prospective randomized multi-center study, it was observed that the ulcer-free interval improved significantly after perforator surgery in patients with a medially located and /or a recurrent venous leg ulcer[22].
Treatment of insufficient perforators may be done classically (open) and endoscopically via the Subfascial Endoscopic Perforating Vein Surgery (SEPS-procedure).
The open perforantectomy according to Linton (gaiter incision) is obsolete because the chance of wound complications is considerable. Therefore, perforantectomies

must now be done scopically [19,23,24]. In the long-term, the SEPS-procedure also has the same chance of healing and recurrence as the Linton-procedure, but with considerably fewer wound complications[25]. There are also publications, which reported no difference in wound healing with or without SEPS[26].
A second procedure (re-SEPS) with good results may be carried out if the SEPS procedure proves incomplete[27].

Conclusions

Level 3	The ulcer-free interval improves significantly after perforantectomy in patients with a medial and/or recurrent venous leg ulcer. *A2* *Van Gent 2004[22]*

Level 2	The SEPS-procedure as a treatment for insufficient venae perforantes in venous leg ulcers has few wound complications, good chances of healing and a low recurrence.The open perforantectomy according to Linton is obsolete. *A2* *Pierik 1997[19]; Sybrandy 2001[25]* *B* *Sato 1999[23]; Stuart 1997[24]*

Other considerations
For the time being it seems that insufficient perforantes in patients with a venous leg ulcer can be adequately treated. In principle, SEPS-procedure is preferred in these situations. Unfortunately, SEPS-procedure may be unsuccessful in some cases. Therefore, it is important that the healer/surgeon subsequently determine whether the patient still must undergo a conventional surgical intervention.

Recommendation 21

A perforantectomy with the SEPS-procedure should be done if an operative intervention is considered for treating venae perforantes insufficiency in patients with a medial and/or a recurrent venous leg ulcer.

5.5 Biopsy

A biopsy from the edge of the wound may rule out the possibility of a malignancy or a malignant degeneration. It should be performed on all the (venous leg) ulcers if healing does not occur.

5.6 Combination of different treatments including sclero-compression therapy

Scientific basis
Considering the fact that isolated insufficiency of venae perforantes and the deep venous system rarely occur, a combination of different surgical interventions is frequently carried out with good results[5,28].
Surgical treatment of the superficial system with a GSV crossectomy and stripping in combination with a perforantectomy has also yielded good results in insufficiency of the deep venous system[6,19].
In medical literature, it has not been shown that sclero-compression therapy effectively contributes to the healing of venous leg ulcers in the case of superficial venous insufficiency. Sclero-compression therapy should then also be considered as an adjuvant therapy[7].

Conclusions

Level 1	The treatment of combined superficial venous insufficiency and insufficiency of the venae perforantes with stripping and SEPS have good results in patients with a venous leg ulcer even when the deep venous system is insufficient. *A1* *Padberg 1999*[28] *A2* *Pierik 1997*[19] *B* *DePalma 1996*[5]

Level 3	Sclero-compression may contribute to the effective treatment of venous leg ulcers. *D* *Clement 1999*[7] *B* *Cabrera 2004*[38]

Recommendation 22

The treatment of first choice for patients with a venous leg ulcer with a combined insufficiency of superficial and perforatory systems is crossectomy and short stripping of the GSV, as well as a perforantectomy according to the SEPS-procedure.

Recommendation 23

The working group is of the opinion that sclero-compression therapy in the case of locally draining varices on the ulcer may speed up wound healing.

Literature

1. SIGN. The care of patients with chronic leg ulcer; a national guideline; 1998.
2. Barwell R, Taylor M, Deacon J, Ghauri AS, Wakely C, Phillips LK, et al. Surgical correction of isolated superficial venous reflux reduces long-term recurrence rate in chronic venous leg ulcers. Eur J Vasc Endovasc Surg 2000;20:363-8.
3. Bello M, Scriven M, Hartshorne T, Bell PR, Naylor AR, London NJ. Role of superficial venous surgery in the treatment of venous ulceration. Br J Surg 1999;86:755-9.
4. Scriven JM, Hartshorne T, Thrush AJ, Bell PR, Naylor AR, London NJ. Role of saphenous vein surgery in the treatment of venous ulceration. Br Surg 1998;85:781-4.
5. DePalma RG, Kowallek DL. Venous ulceration: a cross-over study from nonoperative to operative treatment. J Vasc Surg 1996; 24:788-92.
6. Padberg FT, Pappas PJ, Araki CT, Back TL, Hobson RW. Hemodynamic and clinical improvement after superficial vein ablation in primary combined venous insufficiency with ulceration. J Vasc Surg 1996;24:711-8.
7. Clement DL. Venous ulcer reappraisal: insights from an international task force. J Vasc Res 1999;36:42-7.
8. Masuda EM, Kistner RL. Long term results of venous valve reconstruction: a four- to twenty-one-year follow-up. J Vasc Surg 1994;19:391-403.
9. Raju S, Berry MA, Neglén P. Transcommissural valvuloplasty: technique and results. J Vasc urg 2000;32:969-76.
10. Dalsing MC, Raju S, Wakefield TW, Taheri S. A multicenter, phase I evaluation of cryopreserved venous valve allografts for the treatment of chronic deep venous insufficiency. J Vasc Surg 1999;30:854-66.
11. Lacroix H, Smeets A, Nevelsteen A, Suy R. Classic versus endoscopic

perforating vein surgery: a retrospective study. Acta Chir Belg 1998;98:71-5.

12. Gloviczki P. Subfascial endoscopic perforator vein surgery: indications and results. Vasc Med 1999;4:173-80.
13. Rhodes JM, Gloviczki P, Canton LG. Factors affecting clinical outcome following endoscopic perforator vein ablation. Am J Surg 1998;176:162-7.
14. Baron HC, Saber AA, Wayne M. Endoscopic subfascial surgery for incompetent perforator veins in patients with active venous ulceration. Surg Endosc 2001;15:38-40.
15. Nelzen O. Prospective study of safety, patient satisfaction and leg ulcer healing following saphenous and subfascial endoscopic perforator surgery. Br J Surg 2000;87:86-91.
16. Pierik EGJM, Wittens CHA, Urk van H. Subfascial endoscopic ligation in the treatment of incompetent perforator veins. Eur J Vasc Endovasc Surg 1995;9:38-41.
17. Rhodes JM, Gloviczki P. Endoscopic perforating vein surgery. Surg Clinics North Am 1999;79:667-81.
18. Hauer G, Bergan JJ, Werner A, Mitterhusen M, Nasralla F. Development of endoscopic dissection of perforating veins and fasciotomy for treatment of chronic venous insufficiency. Ann Vasc Surg 1999;13:357-64.
19. Pierik EG, van Urk H, Hop WC, Wittens CH. Endoscopic versus open subfascial division of incompetent perforating veins in the treatment of venous leg ulceration: A randomized trial. J Vasc Surg 1997;26:1049-54.
20. Gloviczki P, Bergan JJ, Menawat SS, Hobson RW, Kistner RL, Lawrence PF, et al. Safety, feasibility, and early efficacy of subfascial endoscopic perforator surgery: a preliminary report from the North American registry. J Vasc Surg 1997;25:94-105.
21. Gloviczki P, Bergan JJ, Rhodes JM, Canton LG, Harmsen S, Ilstrup DM. Mid-term results of endoscopic perforator vein interruption for CVI: lessons learned from the NASEPS registry. J Vasc Surg 1999;29:489-502.
22. Van Gent WB, Witten CHA. Conservatieve versus operatieve behandeling van het ulcus cruris venosum. Een gerandomiseerd multicenter onderzoek. Eindverslag. Rotterdam: Sint Franciscus Gasthuis; 2004.
23. Sato DT, Goff CD, Gregory RT, Walter BF, Gayle RG, Parent FN, et al. Subfascial perforator vein ablation: comparison of open versus endoscopic techniques. J Endovasc Surg 1999;6:147-154.
24. Stuart WP, Adam DJ, Bradbury AW, Ruckley CV. Subfascial endoscopic perforator surgery is associated with significantly less morbidity and shorter hospital stay than open operation (Linton's procedure). Br J Surg 1997;84:1364-5.
25. Sybrandy JE, van Gent WB, Pierik EG, Wittens CH. Endoscopic versus open subfascial division of incompetent perforating veins in the treatment of venous leg ulceration: long-term follow-up. J Vasc Surg 2001;33:1028-32.
26. Scriven JM, Bianchi V, Hartshorne T, Bell PR, Naylor AR, London NJ. A clinical and haemodynamic investigation into the role of calf perforating vein surgery in patients with venous ulceration and deep venous incompetence. Eur J Vasc Endovasc Surg 1998;16:148-52.
27. Kolvenbach R, Ramadan H, Schwierz E. Redone endoscopic perforator surgery: feasibility and failure analysis. J Vasc Surg 1999;30;720-6.
28. Padberg Jr FT. Surgical intervention in venous ulceration. Cardiovasc Surg 1999;7:83-90.
29. Smith JJ, Garratt AM, Guest M, Greenhalgh RM, Davies AH. Evaluating and improving health-related quality of life in patients with varicose veins. J Vasc Surg. 1999; 30: 710-9.
30. Nicolini P, Closure Group. Treatment of primary varicose veins by endovenous obliteration with the VNUS closure system: results of a

prospective multicentre study. Eur J Vasc Endovasc Surg. 2005; 29: 433-9.

31. Myers K, Fris R, Jolley D. Treatment of varicose veins by endovenous laser therapy: assessment of results by ultrasound surveillance. Med J Aust 2006; 185: 199-202.
32. Mundy L, Merlin TL, Fitridge RA, Hiller JE. Systematic review of endovenous laser treatment for varicose veins. Br J Surg 2005; 92: 1189-94.
33. 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.
34. 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.
35. de Waard MM, der Kinderen DJ. Duplex ultrasonography-guided foam sclerotherapy of incompetent perforator veins in a patient with bilateral venous leg ulcers. Dermatol Surg. 2005; 31: 580-3.
36. Zamboni P, Cisno C, Marchetti F, Mazza P, Fogato L, Carandina S et al. Minimally invasive surgical management of primary venous ulcers vs. compression treatment: a randomized clinical trial. Eur J Vasc Endovasc Surg 2003; 25(4):313-318.
37. Barwell JR, Davies CE, Deacon J, Harvey K, Minor J, Sassano A et al. Comparison of surgery and compression with compression alone in chronic venous ulceration (ESCHAR study): randomised controlled trial. Lancet 2004; 363(9424):1854-1859.
38. Cabrera J, Redondo P, Becerra A, Garrido C, Cabrera J, Jr., Garcia-Olmedo MA, Sierra A, Lloret P, Martinez-Gonzales MA. Ultrasound-guided injection of polidocanol microfoam in the management of venous leg ulcers. Arch Dermatol. 2004 Jun;140:667-73.

CHAPTER 6. ORAL MEDICATION

Scientific basis

Various medicines have been used to enhance the process of healing in venous ulcers. These medicines have an effect on edema, hematocriet, increased capillary permeability, inflammation, decreased fibrinolysis, abnormal leukocyte function and transformation of erythrocytes. One may generally state that oral medication without compression therapy is not useful in the treatment of venous ulcers. Oral medication as an addition to topical treatment and compression therapy is highly debated. Treatment of healthy patients with zinc did not prove to be useful[1,2]. Of the various medicines (aspirin and pentoxyfylline) that may influence the blood flow in the microcirculation, there are only a few published studies which in fact also report a possible influence on the duration of healing[3-7]. However, these studies are of moderate quality. In an investigation by Dale, there was no difference in the treatment with or without oral medication[6]. It may generally be concluded that the added value of oral medication has not been proven, but pentoxyfylline and aspirin have a possible additive effect[7]. The role of oral antibiotics in venous ulcers was already described earlier.

Complaints of pain in venous ulcers are often poorly highlighted. There are no reported studies in which different means to alleviate pain have been compared. There is insufficient evidence on the role of other drugs such as Diuretics, Aspirin, Proteoglycan and MPFF.

Conclusion

	The additional value of exclusive oral medication in the treatment of venous ulcers has not been proven sufficiently.

Level 2	*A2* *B* *A1*	*Jull 2002*[7] *Ibbotson 1995*[2] *Coleridge-Smith*[8]

Recommendation 24

The working group is of the opinion that an adequate alleviation of pain deserves attention.

Literature

1. Wilkinson EAJ, Hawke CI. Oral zinc for arterial and venous leg ulcers (Cochrane Review) In: The Cochrane Library, Issue 4, 2001. Oxford: Update software.
2. Ibbotson SH, Layton AM, Davies JA, Goodfield. The effect of aspirin on haemostatic activity in the treatment of chronic venous leg ulceration. Br J Dermatol 1995;132:422-6.
3. Colgan M-P, Dormandy JA, Jones PW, Schraibman IG, Shanik DG, Young RA. Oxpentifylline treatment of venous ulcers of the leg. BMJ 1990;300:972-4.
4. Layton M, Ibbotson SH, Davies JA, Goodfield MJ. Randomised trial of oral aspirin for chronic venous leg ulcers. The Lancet 1994;344:164-5.
5. Falanga V, Fujitani RM, Diaz C, et al. Systemic treatment of venous leg ulcers with high doses of pentoxifylline: efficacy in a randomized, placebo controlled trial. Wound Rep Reg 1999:208-13.
6. Dale JJ, Ruckley CV, Harper DR, Gibson B, Nelson EA, Prescott RJ. Randomised, double blind placebo controlled trial of pentoxifylline in the treatment of venous leg ulcers. BMJ 1999;319:875-8.
7. Jull A, Waters J, Arroll B. Pentoxifylline for treatment of venous leg ulcers: a systematic review. Lancet 2002;359:1550-4.
8. Coleridge-Smith P, Lok C, Ramelet AA. Venous leg ulcer: a meta-analysis of adjunctive therapy with micronized purified flavonoid fraction. Eur J Vasc Endovasc Surg. 2005 Aug; 30(2): 198-208.

CHAPTER 7. AFTER TREATMENT

Compression for the purpose of preventing recurrence of a venous leg ulcer
Scientific basis
There are no randomized studies in which compression and no compression were compared. One can only speak of indirect proof because compliance may be poor.
In systemic reviews, compression was recommended as an after-treatment for preventing recurrence[1-3], whereby the highest pressure that the patient can tolerate is applied[1], but well adjusted to the condition of the patient[2]. After the venous ulcer had healed, a recurrence was observed in 32% of those wearing a class 2 stocking and in 21% of those wearing a class 3 stocking after 3-5 years[4]. Class 3 stockings were superior, but were tolerated less well than class 2 stockings[3].
In a non-comparative clinical investigation, 53 patients in whom venous leg ulcer was closed by using an Ulcercare® bandage stocking system (10-15 mm Hg understocking + a 30 mm Hg stocking with a zip) were treated with the same stockings after the ulcer was healed[3]. In the group that wore stockings (almost one-half) only 4% developed a recurrent ulcer after 6 months, whereas 79% of those who did not or only occasionally wore the stockings developed a recurrent ulcer.

In another study, 188 patients with recently closed ulcers were mostly prescribed ready-made class 2 MECH[5]. A recurrent ulcer was observed in 26% of the patients after 1 year and in 31% of the patients after 1.5 years. A risk factor, among others, was not wearing the MECH.
In most cases it will be decided to prescribe MECH as an after treatment. It is important to pre-select the correct type of MECH for the patient. A program of requirements, which supports making a correct decision, has been compiled for this purpose[6].
The prophylactic use of compression therapy in patients with previous venous ulcers has clearly been shown to be cost-effective. This means that it is much cheaper to prescribe adequate medical compression hosiery after ulcers have healed than to cure recurrent ulcers[7].

Conclusion

Level 2	Compression therapy should be given after a venous leg ulcer has healed. Compression with high-pressure MECH (class 3) is better for preventing recurrence than with low-pressure MECH (class 2), but is tolerated less well. *A1* *Nelson 2001[1]; Agus 2001a[2]; NZGG 1999[3]; Agus 2001b[4]*

Recommendation 25

Compression therapy with Medical Elastic Compression Hosiery (MECH), which exerts as much pressure as possible, should be prescribed to prevent recurrence after a venous leg ulcer has healed.

7.2 Ablation of superficial refluxes for preventing the recurrence of a venous leg ulcer

Scientific basis
When the venous ulcer has epithelialized after conservative therapy, the patient is not cured because the pathophysiological background that led to ulceration is still present. This fact explains the high recurrence rate ranging between 26-69% in 12 months[1]. Ablation of venous refluxes by using surgery or endovenous techniques may normalize the disturbed venous hemodynamics and prevent ulcer recurrence.
It has been shown that most patients with chronic venous ulcers will benefit from simple venous surgery in addition to conventional compression treatment in an effort to reduce the recurrence of ulcers within 12 months[8].

Conclusion

Level 2	Ablation of refluxes in the great saphenous vein by surgery reduces the recurrence of ulcers within 12 months. *A2* *Barwell 2004[8]*

Recommendation

Ablation of superficial refluxes by surgery, by endovenous methods or by (foam-) sclerotherapy should be considered in all cases.

Literature

1. Nelson EA, Bell-Syer SEM, Cullum NA. Compression for preventing recurrence of venous ulcers (Cochrane Review) In: The Cochrane Library: issue 4: 2001.Oxford.

2. Agus GB, Allegra C, Arpaia G, Botta G, Cataldi A, Gasbarro V, et al. Guidelines on compression therapy. Acta Phlebologica 2001a; suppl. 1:1-24.
3. New Zealand Guidelines Group, the Royal New Zealand College of General Practitioners. Care of people with chronic leg ulcers. An evidence based guideline 1999.
4. Agus GB, Allegra C, Arpaia G, Botta G, Cataldi A, Gasbarro V, et al. Guidelines for the diagnosis and treatment of diseases of the veins and lymphatic vessels: Evidence-based report by the Italian College of Phlebology. Int angiol 2001b;20 Suppl 2:6-27.
5. Franks PJ, Oldroyd MI, Dickson D, Sharp EJ, Moffatt CJ. Risk factors for leg ulcer recurrence: a randomized trial of two types of compression stocking. Age Ageing 1995;24(6):490-4.
6. Hulpmiddelen Kompas Therapeutisch Elastische Kousen. Amstelveen: College voor Zorgverzekeringen; 2002.
7. Korn P, Patel ST, Heller JA, Deitch JS, Krishnasastry KV, Bush HL, et al. Why insurers should reimburse for compression stockings in patients with chronic venous stasis. J Vasc Surg. 2002 May;35:950-7.
8. Barwell JR, Davies CE, Deacon J, Harvey K, Minor J, Sassano A et al. Comparison of surgery and compression with compression alone in chronic venous ulceration (ESCHAR study): randomised controlled trial. Lancet 2004; 363(9424):1854-1859.

CHAPTER 8. LIFE STYLE

Introduction
In this chapter, the importance of advice on the life style of the patients during the treatment and aftercare phase of leg ulcer is discussed. A review of studies on this subject is first given. In the second paragraph a number of examples taken from practice are presented.

8.1 Life style in medical literature

Scientific basis
Little proof of the influence of life style on the prevention and healing of leg ulcers is encountered in medical literature. In their publication, Kunimoto et al presented 12 recommendations, which stated the best clinical interventions and expert opinion supplemented by available investigation. There was one recommendation that was directly related to the life style of the patient, namely "consultation with revalidation experts to maximize activity and mobility". Limitation in the movement of the ankle leads to an increase in the venous pressure and development of an edema in patients with chronic venous insufficiency. Walking improves the calf muscle pump function[1].
The nutritional status of patients with leg- and foot ulcers was evaluated in relation to social demographic factors such as mobility, physical activity, ulcer history and problems related to the ulcer. In 51% of the cases there was venous insufficiency, in 9% of the cases there was an arterial insufficiency and in 11% of the cases there was a combined venous-arterial insufficiency. The remaining 29% of the causes could to ascribed to afflictions such as diabetes, trauma or others. The patients (20 men and 50 women) lived alone and received a first line treatment. The "Mini Nutritional Assessment" (MNA) was used to establish the nutritional status. According to the MNA, 32 patients ran the risk of malnutrition and two of them were malnourished. The patients who were at risk generally lived alone and depended more on help (aids) from mobility and home care organizations than those who were well-fed. There were no significant differences between the number and the duration of open

ulcers in well-fed patients and those who were at risk of malnutrition. This investigation showed that the risk of malnutrition was a general problem among these 70 elderly patients with leg- and foot ulcers[2].
The healing of ulcers, the recurrence of ulcers, the nutritional status and the living conditions of the elderly patients with leg ulcers were investigated in a subsequent study. Of the 70 patients who were involved in the investigation in 1999, 61% were still alive in 2000 and 88% of these participated in the follow-up study. The ulcers had healed in 50% of the patients, amputation had been necessary in 5% and open ulcers were still present in 45% (in 6 of the patients the previous ulcers had not yet healed and new ulcers had again developed in 11 elderly patients). The average MNA scores were lowered as were the average ADL scores and mobility in the patients with open ulcers, but not among the patients whose the ulcers had healed. The patients with healed ulcers had higher average scores on social interaction than those with open ulcers and the average scores on quality of the surrounding were significantly higher. The results showed that there was a possible relationship between nutrition and the living conditions and the healing of leg ulcers[3].
The aim of the study by Wipke-Travis et al was to investigate the nutrition, the tissue oxygen and the healing of venous leg ulcers. The nutrition status, the physical dimensions, the biochemical indices, the two three-day diet reports and the level of tissue oxygen from the 25 participating individuals were recorded. The results of this study showed that there were no statistically significant relationships between the biochemical nutrition indices, tissue oxygen and healing[4].
The prevalence of malnutrition is high in patients suffering from leg ulcers. The nutritional status may be a marker of wound tendency and a risk factor for delayed wound healing[8].

Conclusion

Level 3	There is a possible relationship between nutrition, living conditions and the healing of leg ulcer. *C Wissing 1999[2]; 2001[3]*

Recommendation 26

An adequate patient care in the treatment of venous leg ulcers also includes optimization of the nutritional status.

8.2 Information and advice

In 1985, a project was started in the Amsterdam region with the aim of improving the quality and/or reducing the costs whereby it was looked at whether it was possible to bring about a change in the existing care and treatment patterns for disorders which required a prolonged stay in the hospital. The results of the project were used to develop a care protocol. Leg ulcers were selected as one of the disorders. A first protocol was ready in 1987. An update followed in 2000[5].
Considerable attention was paid to information and advice on life style in this protocol.

In any case the patient should receive information on:

- Causes of the ulcer
- Treatments
- The necessity to treat other underlying diseases

Advice must also be given on:

- The necessity of regular movement of the foot and the leg
- Well-fitting footwear
- Skin and nail care

It also emerged from other experiments in the Netherlands that providing information on the treatment of "open ulcers" was an important issue. The advice, which corroborates the advice in the Amsterdam protocol (protocols of the Foundation for Transmural care The Hague e.o., Medical Center Molendael, Baarn, Lorentz Hospital, Zeist, Home care program of KITTZ, Groningen) is cited in the various care booklets.
Providing information and advice is also high on the international agenda. It was once again emphasized in investigations by Seiter et al that movement was very important in the treatment of chronic venous insufficiency.[6] In their study, Blair et al mentioned various risk factors including overweight, inactivity, the use of walking aids and reduced ankle movement in the development of new ulcers[7].
Evaluation of whether the advice and counselling provided is followed leads to a better compliance with the therapy.

Conclusion

Level 4	Adequate information and advice on life style provide an important contribution to the prevention and the treatment of venous leg ulcers. *D Hulsebosch 1993[5]; Seiter 2001[6]; Blair 2001[7]*

Recommendation 27

The working group is of the opinion that providing information and advice concerning life style is indispensable in the treatment of leg ulcers.

Attention must at least be paid to the following points:

- Avoiding immobility
- Encouraging the use of the calf muscle pump (walking, adequate footwear)
- Avoiding (developing) overweight
- Encouraging adequate nutrition
- Discouraging smoking

Literature

1. Kunimoto B, Cooling M, Gulliver W, Houghton P, Orsted H, Sibbald RG. Best practices for the prevention and treatment of venous leg ulcers, Ostomy Wound Management, 2001;47(2):34-50.
2. Wissing U, Unosson M. The relation between nutritional status and physical activity, ulcer history and ulcer-related problems in patients with leg and foot ulcers. Scandinavian journal of caring sciences, 1999;13(2):123-8.
3. Wissing U, Unosson M. A follow-up study of ulcer healing, nutrition, and life-situation in elderly patients with leg ulcers, The journal of nutrition, health and aging, 2001; 5(1): 37-42.
4. Wipke-Tevis DD, Stotts NA, Nutrition, tissue oxygenation and healing of venous leg ulcers. J Vas Nurs 1998;16(3):48-56.
5. Hulsbosch HJ. Leg Ulcers: diagnosis and treatment. Edited by W. Westerhof. Elsevier Science Publishers; 1993.
6. Seiter H, Boes K. Influences of several foot-muscle pump supporting devices on the venous flow velocity during a scheduled walking program. In: Proceedings of the 14th World Congress of Union Internationale de Phlebologie; 2001 Sep 9-14; Rome, Italy.
7. Blair SD, Hamsho A. Velthysen G, Mansell I. Factors influencing recurrence of venous ulcers during long term follow-up. In: Proceedings of the 2nd international congress of the European Venous Forum; 2001 Sep 13-14; Rome, Italy.

8. Legendre C, Debure C, Meaume S, Lok C, Senet P. Valeur pronostique de la denutrition proteique sur la cicatrisation des ulcers de jambe. Ann Dermatol Venereol 2005, 132 ; 9S46-7.

SOP for creation of European Dermatology Guidelines

Step	Responsible	Task	Months duration
1	EDF Guidelines Committee (EDF-GC)	Decision of topic of specific guideline	Ø
2	EDF Board	Confirmation of the choice and level of guideline (S1, S2 or S3) plus suggestion to the Guideline Committee of potential chairmen and subcommittee members.	0,5
3	EDF Guidelines Committee	Foundation of subcommittee for specific guidelines. Nomination of EDF members (50 %) as well as identification of possible EADV members (25 % of members for the subcommittee) who could work within the subcommittee. Chairman of EDF guideline committee asks EADV president for approval. Finally nomination of a chairperson of the subcommittee by the group.	at EDF Meeting
4	EDF-GSubC	Development of a business plan (see attachment)	1
5	EDF Board	Confirmation of business plan and signature of the contract for financial support of guideline	1
6	EDF Guidelines Subcommittee (EDF-GSubC)	Identify all existing guidelines for the specific guideline (active process: literature survey plus contact to Dermatological Societies)	1
7	EDF Guidelines Subcommittee	Select the guidelines with highest quality. Criteria for selection: 1. Availability of strength of evidence 2. Availability of strength of recommendation 3. Evidence of mechanics of literature review (adhere to the recommendations of the Cochrane collaboration. These standards should assure high quality for the systematic literature search as well as for the critical appraisal of the papers. For further information see http://www.cochrane.org/crgprocedures/chapter4/1.htm and documents available at EDF Guidelines Secretariat (Mrs. Janine Schweiger, janine.schweiger@charite.de)	1
8	EDF Guidelines Subcommittee	Identification/nomination of additional 50 % EDF members for the EDF-GSubC from amongst the authors of the best guidelines	0,5
9	Chairperson of Subcommittee	Consider involvement of other disciplines and patients´ organisations	1
10	EDF Guidelines Subcommittee	Meet 1. to decide the author of the first draft (normally the chairperson of the subcommittee) and to discuss the present guidelines, their strengths and weaknesses 2. 6 months later to discuss the draft (consensus conference)	6
11	Chairperson of Subcommittee	Circulate the guideline draft to national dermatological societies for comments	2
12	Guidelines Subcommittee	Circulate final version for approval among members of the guideline subcommittee	1
13	Chairperson of	Deliver final version for comments to EDF guideline committee	2

	Subcommittee	chairperson, who forwards it to EADV Board and to UEMS	
14	EDF Guidelines Committee	Review and comment guideline	1
15	EDF Guidelines Committee chairperson	Send guideline for official approval to UEMS (formal approval)	2
16	EDF secretary	Distribute guideline for in advance information to EDF members and National Dermatological Societies	1
17	EDF	Publication 1. on EDF homepage 2. in European dermatological journals 3. If publication in other national and international journals is requested by the respective society, this will be encouraged by the EDF	6