Guidelines for the treatment of venous ulcers

Martin C. Robson, MD[1,2]; Diane M. Cooper, PhD, RN[1,3]; Rummana Aslam, MD[4]; Lisa J. Gould, MD, PhD[5]; Keith G. Harding, MBChB, MRCGP, FRCS[6]; David J. Margolis, MD, MSCE, PhD[7]; Diane E. Ochs, RN[2]; Thomas E. Serena, MD[8]; Robert J. Snyder, DPM[9]; David L. Steed, MD[10]; David R. Thomas, MD[11]; Laurel Wiersma-Bryant, RN, BC, ANP[12]

1. Co-chaired this panel
2. University of South Florida, Tampa, FL
3. Healthpoint Ltd., Fort Worth, TX
4. University of California, San Francisco, CA
5. University of Texas Medical Branch, Galveston, TX
6. University of Cardiff, Cardiff, Wales, UK
7. University of Pennsylvania, Philadelphia, PA
8. Private practice, Warren, PA
9. Private practice, Tamarac, FL
10. University of Pittsburgh, Pittsburgh, PA
11. St. Louis University, St. Louis, MO, and
12. Washington University, St. Louis, MO

An advisory panel of academicians, private practice physicians, podiatrists, nurse clinicians, research nurses, industrial scientists, and an epidemiologist was chosen to develop guidelines for the treatment of venous ulcers of the lower extremity.

METHODS

Previous guidelines, meta-analyses, PubMed, MEDLINE, EMBASE, The Cochrane Database of Systematic Reviews, recent review articles of venous ulcer treatment, and the Medicare/CMS consensus of usual treatment of chronic wounds were all reviewed for evidence. Guidelines were formulated, the underlying principle(s) enumerated, and evidence references listed and coded. The code abbreviations for the evidence citations were as follows:

STAT	Statistical analysis, meta analysis, consensus statement by commissioned panel of experts
RCT	Randomized clinical trial
LIT REV	Literature review
CLIN S	Clinical case series
RETRO S	Retrospective series review
EXP	Experimental laboratory or animal study
TECH	Technique or methodology description
PATH S	Pathological series review

There were major differences between our approach to evidence citations and past approaches to evidence-based guidelines. Most past approaches relied only on publications regarding clinical human studies. Laboratory or animal studies were not cited. We have used well-controlled animal studies that present proof of principle, especially when a clinical series corroborated the laboratory results. It was also clear that principles that have been validated for other chronic wound types often are applicable to venous ulcers. Therefore, evidence was sometimes cited that was not specific for venous ulcers. Because of these variations, a different system was used to grade the evidence weight supporting a given guideline. The level strength of evidence supporting a guideline is listed as Level I, Level II, or Level III. The guideline levels are:

- *Level I*: Meta-analysis of multiple RCTs or at least two RCTs support the intervention of the guideline. Another route would be multiple laboratory or animal experiments with at least two clinical series supporting the laboratory results.
- *Level II*: Less than Level I, but at least one RCT and at least two significant clinical series or expert opinion papers with literature reviews supporting the intervention. Experimental evidence that is quite convincing, but not yet supported by adequate human experience is included.
- *Level III*: Suggestive data of proof of principle, but lacking sufficient data such as meta-analysis, RCT, or multiple clinical series.
- *NB*: The suggestion in the guideline can be positive or negative at the proposed level (e.g., meta-analysis and two RCTs stating intervention is not of use in treating venous ulcers).

RESULTS

Guidelines have been formulated in eight categories for the treatment of venous ulcers of the lower extremities. The categories are:

- Diagnosis
- Compression
- Infection Control
- Wound Bed Preparation
- Dressings
- Surgery
- Adjuvant Agents (Topical, Device, Systemic)
- Long-Term Maintenance

Each of the separate guidelines underwent a Delphi consensus among the panel members to be critically evaluated. There was a consensus of at least ten panel members on each individual guideline. The majority of the guidelines had unanimous concurrence. The draft guidelines were presented at an open conference on October 3, 2005. Following the conference and audience discussion, a period of one month was allowed for written comments and submission of additional evidence literature. The draft guidelines were then modified, taking into consideration

all verbal and written comments. The resultant Guidelines for the Treatment of Venous Ulcers follows.

GUIDELINES FOR THE *DIAGNOSIS* OF LOWER EXTREMITY VENOUS ULCERS

Preamble: Ulcers of the lower extremity may be caused by a variety of conditions. Elevation of ambulatory venous pressure (venous hypertension) is the most common. However, as treatment of the ulcer may vary depending on ulcer etiology, it is paramount that a correct diagnosis is made before treatment.

Guideline #1.1: Gross arterial disease should be ruled out by establishing that pedal pulses are present on physical examination and/or that the ankle : brachial index (ABI) is > 0.8. (Any ABI less than 1.0 suggests a degree of vascular disease and compression therapy is usually considered to be contraindicated with an ABI < 0.7.) In elderly patients, patients with diabetes mellitus, or patients with an ABI > 1.2, a toe : brachial index of > 0.6 or a trans-cutaneous oxygen partial pressure of > 30 mmHg in the region of the ulcer may help to suggest an adequate arterial flow (Level I).

Principle: Venous ulcers can exist in the presence of mixed arterial/venous pathology. However, treatment of only the elevated venous pressure will not succeed when significant arterial disease is present.

Evidence:

1. Porter JM, Moneta GL. International consensus committee on chronic venous disease: reporting standards in venous disease: an update. *J Vasc Surg* 1995; 21: 635–45 [STAT].
2. Beebe HG, Bergan JJ, Bergqvist D et al. Classification and grading of chronic venous disease in the lower limbs: a consensus statement. *Eur J Vasc Endovasc Surg* 1996; 12: 487–92 [STAT].
3. Beebe HG, Bergan JJ, Bergqvist D et al. Classification and grading of chronic venous disease in the lower limbs: a consensus statement. *Internat Angiology* 1995; 14: 197–201 [STAT].
4. Porter JM, Rutherford RB, Clagett GP et al. Reporting standards in venous disease. *J Vasc Surg* 1988; 8: 172–81 [STAT].
5. Kjaer ML, Mainz J, Soerensen LT et al. Clinical quality indicators of venous leg ulcers: development, feasibility, and reliability. *Ostomy/Wound Manage* 2005; 51: 64–74 [STAT].
6. Trent JT, Falabella A, Eaglstein WH et al. Venous ulcers: pathophysiology and treatment options. *Ostomy/Wound Manage* 2005; 51: 38–54 [LIT REV].
7. Robson MC, Hanfnt J, Garner W et al. Healing of chronic venous ulcers is not enhanced by the addition of topical repifermin (KGF-2) to standardized care. *J Appl Res* 2004; 4: 302–11 [RCT].
8. Hirsch AT, Criqui MH, Treat-Jacobson D et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA* 2001; 286: 1317–24 [CLIN S].

Guideline #1.2: Many definitions have been used to diagnose venous leg ulcers including clinical history and examination, invasive, and noninvasive testing. It is important to understand how the diagnosis was made and to understand the limitations of the method. Color duplex ultrasound scanning performed with proximal compression or a Valsalva maneuver is useful in providing anatomic and physiologic data helping to confirm a venous etiology for the leg ulcer (Level I).

Principle: Although clinical history and physical examination can be very suggestive of a venous etiology of the lower extremity ulcer after insufficient arterial inflow has been eliminated, a definitive diagnosis of the venous disease is desirable. This is not always possible. When using various tests to document venous disease, it is paramount that the information needed by the clinician be clearly communicated to the test performer.

Evidence:

1. Porter JM, Moneta GL. International consensus committee on chronic venous disease. Reporting standards on venous disease: an update. *J Vasc Surg* 1995; 21:635–45 [STAT].
2. Beebe HG, Bergan JJ, Bergqvist D et al. Classification and grading of chronic venous disease in the lower limbs: a consensus statement. *Eur J Vasc Endovasc Surg* 1996; 12: 487–92 [STAT].
3. Beebe HG, Bergan JJ, Bergqvist D et al. Classification and grading of chronic venous disease in the lower limbs: a consensus statement. *Int Angiol* 1995; 14: 197–201 [STAT].
4. Porter JM, Rutherford RB, Clagett GP et al. Reporting standards in venous disease. *J Vasc Surg* 1988; 8: 172–81 [STAT].
5. Kjaer ML, Mainz J, Soerensen LT et al. Clinical quality indicators of venous leg ulcers: development, feasibility, and reliability. *Ostomy/Wound Manage* 2005; 51: 64–74 [STAT].
6. Mekkes JR, Loots MA, VanDerWal AC et al. Causes, investigation, and treatment of leg ulceration. *Br J Dermatol* 2003; 148:388–401 [LIT REV].

Guideline #1.3: Patients presenting with an apparent venous ulcer and who are suspected of having sickle cell disease should have a sickle cell prep and a hemoglobin electrophoresis (Level II).

Principle: Patients with homozygous, heterozygous, or trait sickle cell hemoglobin can present with lower extremity ulcers resembling venous ulcers.

Evidence:

1. Karayalcin G, Rosner F, Kim KY et al. Sickle cell anemia—clinical manifestations in 100 patients and review of the literature. *Am J Med Sci* 1975; 269: 51–68 [LIT REV].
2. Wolfort FG, Krizek TJ. Skin ulceration in sickle cell anemia. *Plast Reconstr Surg* 1969; 43: 71–7 [CLIN S].

Guideline #1.4: Apparent venous ulcers that have been open continuously without signs of healing for 3 months

or that do not demonstrate any response to treatment after 6 weeks should be biopsied for histological diagnosis (Level III).

Principle: Malignancy, vasculitis, collagen-vascular diseases, and dermal manifestations of systemic diseases may present as ulcers on the lower extremity.

Evidence:

1. Hansson C, Andersson E. Malignant skin lesions on the legs and feet at a dermatological leg ulcer clinic during five years. *Acta Derm Venereol* 1997; 78: 147–8 [CLIN S].
2. Snyder RJ, Stillman RM, Weiss SD. Epidermoid cancers that masquerade as venous ulcer disease. *Ostomy/Wound Manage* 2003; 49: 63–6 [CLIN S].
3. Mekkes JR, Loots MA, VanDerWal AC et al. Causes, investigation, and treatment of leg ulceration. *Br J Dermatol* 2003; 148: 388–01 [LIT REV].
4. Chakrabarty A, Phillips T. Leg ulcers of unusual causes. *Int J Low Extrem Wounds* 2003; 21: 207–16 [LIT REV].

Guideline #1.5: Apparent venous ulcers, as well as all wounds, that are excessively painful and that progressively increase in size after debridement and/or despite treatment should be considered for other diagnoses such as pyoderma gangrenosum, IgA monoclonal gammopathies, Wegener's granulomatosis, cutaneous chronic granulomatous disease, and mycobacterial or fungal etiologies. This suspicion should be especially high if the ulcer is darker in color, has blue/purple borders, or if the patient has a systemic disease such as Crohn's disease, ulcerative colitis, rheumatoid arthritis, collagen vascular diseases, leukemia, or immunosuppression (Level II).

Principle: Leg ulcers that worsen in size and symptoms despite treatment, or do not show any improvement over 4 weeks of treatment, should raise suspicion that the ulcer etiology is not venous in origin or that the therapy needs to be re-evaluated. At this point, specific cultures for mycobacteria and/or fungi are useful, as biopsies for histology.

Evidence:

1. Reichrath J, Bens G, Bonowitz A et al. Treatment recommendations for pyoderma gangrenosum: an evidence-based review of the literature based on more than 350 patients. *J Am Acad Dermatol* 2005; 53: 273–83 [STAT].
2. Su WP, Schroeter AL, Perry HO et al. Histopathologic and immunopathologic study of pyoderma gangrenosum. *J Cutan Pathol* 1986; 13: 323–30 [PATH S].
3. Hickman JG, Lazurus GS. Pyoderma gangrenosum: a reappraisal of associated systemic diseases. *Br J Dermatol* 1980; 102: 235–7 [LIT REV].
4. Wines N, Wines M, Ryman W. Understanding pyoderma gangrenosum: a review. *Med Gen Med* 2001; 3: 6–12 [STAT].
5. Bennett ML, Jackson JM, Jorizzo JL et al. Pyoderma gangrenosum. A comparison of typical and atypical forms with an emphasis on time to remission. Case review of 86 patients from 2 institutions. *Medicine (Baltimore)* 2000; 79: 37–46 [CLIN S].

GUIDELINES FOR *LOWER EXTREMITY COMPRESSION* FOR TREATMENT OF VENOUS ULCERS

Preamble: Venous ulceration results from an elevated ambulatory venous pressure (venous hypertension). This frequently causes edema of the limb. External compression has been the mainstay to combat these problems.

Guideline #2.1: The use of a Class 3 (most supportive) high-compression system (three layer, four layer, short stretch, paste-containing bandages, e.g., Unna's boot, Duke boot) is indicated in the treatment of venous ulcers. Although these modalities are similar in effectiveness, they can differ significantly in comfort and cost. The degree of compression must be modified when mixed venous/arterial disease is confirmed during the diagnostic work-up (Level I).

Principle: Venous ulcer healing is increased when adequate compression is applied to the lower extremity.

Evidence:

1. Cullum N, Nelson EA, Fletcher AW, Sheldon TA. Compression for venous leg ulcers. *The Cochrane Database of Systematic Reviews*. (2001 Issue 2) The Cochrane Collaboration. John Wiley & Sons Ltd. [STAT, 23 RCT].
2. Ennis WJ, Meneses P. Standard, appropriate, and advanced care and medical-legal considerations: part two—venous ulcerations. *Wounds* 2003; 15: 107–22 [LIT REV].
3. Burton CS. Treatment of leg ulcers. *Dermatol Clin* 1993; 11: 315–23 [TECH].
4. Falanga V. Care of venous ulcers. *Ostomy/Wound Manage* 1999; 45 (Suppl. 1A): 33S–43S [LIT REV].
5. Robson MC, Hanfnt J, Garner W et al. Healing of chronic venous ulcers is not enhanced by the addition of topical repifermin (KGF-2) to standardized care. *J Appl Res* 2004; 4: 302–11 [RCT].
6. DePalma RG, Kowallek D, Spence RK et al. Comparison of costs and healing rates of two forms of compression in treating venous ulcers. *Vasc Surg* 1999; 33: 683–90 [RCT].

Guideline #2.2: Intermittent pneumatic pressure (IPC) can be used with or without compression dressings and can provide another option in patients who cannot or will not use an adequate compression dressing system (Level I).

Principle: Intermittent pressure stimulates venous return and can be utilized when constant compression is not tolerated.

Evidence:

1. Smith PC, Sarin S, Hasty J et al. Sequential gradient pneumatic compression enhances venous ulcer healing: a randomized trial. *Surgery* 1990: 108: 871–5 [RCT].
2. Rowland, J. Intermittent pump versus compression bandages in the treatment of venous leg ulcers. *Aust NZ J Surg* 2000; 70: 110–3 [RCT].
3. Ennis WJ, Meneses P. Standard, appropriate, and advanced care and medical-legal considerations: part

two—venous ulcerations. *Wounds* 2003; 15: 107–22 [LIT REV].

Because venous hypertension is an ongoing condition, a degree of compression therapy should be continued constantly and forever. (see Long-Term Maintenance Guidelines.)

GUIDELINES FOR *INFECTION CONTROL* IN THE TREATMENT OF VENOUS ULCERS

Preamble: Infection results when the bacteria : host defense equilibrium is upset in favor of the bacteria. Infection plays various roles in the etiology, healing, operative repair, and complications of venous ulcers.

Guideline #3.1: Remove all necrotic or devitalized tissue by sharp, enzymatic, mechanical, biological, or autolytic debridement (Level I). (Detailed discussion of debridement is in Wound Preparation Guidelines.)

Principle: Necrotic tissue is laden with bacteria while devitalized tissue impairs the body's ability to fight infection and serves as a pabulum for bacterial growth.

Evidence:

1. Edlich RF, Rodeheaver GT, Thacker JG et al. Technical factors in wound management. In Dunphy, JE, Hunt, TK, editors. *Fundamentals of Wound Management in Surgery*. South Plainfield, NJ: Chirurgecom, 1977 [EXP].
2. Bradley M, Cullum N, Sheldon T. The debridement of chronic wounds: a systematic review. *Health Tech Assess* 1999; 3(17 Part 1): 1–78 [STAT].
3. Steed D, Donohue D, Webster M et al. Effect of extensive debridement and rhPDGF-BB (Becaplermin) on the healing of diabetic foot ulcers. *J Am Coll Surg* 1996; 183: 61–4 [RCT].
4. Witkowski JA, Parrish LC. Debridement of cutaneous ulcers: medical and surgical aspects. *Clin Dermatol* 1992; 9: 585–91 [LIT REV].
5. Falanga V. Wound bed preparation and the role of enzymes: a case for multiple actions of therapeutic agents. *Wounds* 2002; 14: 47–57 [LIT REV].
6. Hamer MI, Robson MC, Krizek TJ et al. Quantitative bacterial analyses of comparative wound irrigations. *Ann Surg* 1975; 181: 819–22 [EXP].
7. Saap LJ, Falanga V. Debridement performance index and its correlation with complete closure of diabetic foot ulcers. *Wound Rep Reg* 2002; 10: 354–9 [RCT].
8. Davies CE, Turton G, Woolfry G et al. Exploring debridement options for chronic venous ulcers. *Br J Nurs* 2005; 14: 393–7 [LIT REV].

Guideline #3.2: If infection is suspected in a debrided ulcer, or if epithelialization from the margin is not progressing within 2 weeks of debridement and initiation of compression therapy, determine the type and level of infection in the debrided ulcer by tissue biopsy or by a validated quantitative swab technique (Level II).

Principle: High levels of bacteria $\geq 1\times10^6$ CFU/g of tissue or any tissue level of beta hemolytic streptococci impede the various wound-healing processes and have been demonstrated to impede spontaneous healing and surgical closure of venous ulcers. Cultures should be performed to isolate both aerobic and anaerobic bacteria.

Evidence:

1. Robson MC, Stenberg BD, Heggers JP. Wound healing alterations caused by infection. *Clin Plast Surg* 1990; 17: 485–92 [LIT REV].
2. Robson MC. Wound infection: a failure of wound healing caused by an imbalance of bacteria. *Surg Clin North Am* 1997; 77: 637–50 [LIT REV].
3. Lookingbill DP, Miller SH, Knowles RC. Bacteriology of chronic leg ulcers. *Arch Dermatol* 1978; 114: 1765–8 [RCT].
4. Tobin GR. Closure of contaminated wounds: biologic and technical considerations. *Surg Clin North Am* 1984; 64: 639–52 [LIT REV].
5. Heggers JP. Variations on a theme. In: Heggers JP, Robson MC, editors. *Quantitative Bacteriology: Its Role in the Armamentarium of the Surgeon*. Boca Raton: CRC Press, 1991: 15–23 [TECH].
6. Levine NS, Lindberg RB, Mason AD et al. The quantitative swab culture and smear: a quick method for determining the number of viable aerobic bacteria in open wounds. *J Trauma* 1976; 16: 89–94 [TECH].
7. Nystrom PO. The microbiological swab sampler—a quantitative experimental investigation. *Acta Pathol Microbiol Scand* 1978; 86B: 361–7 [TECH].
8. Volenec FJ, Clark GM, Manni MM et al. Burn wound biopsy bacterial quantification: a statistical analysis. *Am J Surg* 1979; 138: 695–8 [STAT].
9. Stephens P, Wall JB, Wilson MJ et al. Anaerobic cocci populating the deep tissues of chronic wounds impair cellular wound healing responses in vitro. *Br J Dermatol* 2003; 148: 456–66 [CLIN S].
10. Schraibman IG. The significance of beta-haemolytic streptococci in chronic leg ulcers. *Ann R Coll Surg Engl* 1990; 72: 123–4 [CLIN S].

Guideline #3.3: For ulcers with $\geq 1\times10^6$ CFU/g of tissue or any tissue level of beta hemolytic streptococci following adequate debridement, decrease the bacterial level with topical antimicrobial therapy. Once in bacterial balance, discontinue the use of the topical antimicrobial agent to minimize any possible cytotoxic effects due to the antimicrobial agent or emergence of bacterial resistance to the agent (Level I).

Principle: Systemically administered antibiotics do not effectively decrease bacterial levels in granulating wounds; however, topically applied antimicrobials can be effective.

Evidence:

1. Robson MC. Wound infection: a failure of wound healing caused by an imbalance of bacteria. *Surg Clin North Am* 1997; 77: 637–50 [LIT REV].
2. Bishop JB, Phillips LG, Mustoe TA et al. A prospective randomized evaluator-blinded trial of two potential wound healing agents for the treatment of venous stasis ulcers. *J Vasc Surg* 1992; 16: 251–7 [RCT].

3. Lookingbill DP, Miller SH, Knowles RC. Bacteriology of chronic leg ulcers. *Arch Dermatol* 1978; 114: 1765–8 [RCT].
4. Fumal I, Braham C, Paquet P et al. The beneficial toxicity paradox of antimicrobials in leg ulcer healing impaired by a polymicrobial flora: a proof-of-concept study. *Dermatology* 2002; 204 (Suppl. 1): 70–4 [RCT].
5. Robson MC, Mannari RJ, Smith PD et al. Maintenance of wound bacterial balance. *Am J Surg* 1999; 178: 399–402 [RCT].
6. Schraibman IG. The significance of beta-haemolytic streptococci in chronic leg ulcers. *Ann R Coll Surg Engl* 1990; 72: 123–4 [CLIN S].
7. Halbert AB, Stacey MC, Rohr JB et al. The effect of bacterial colonization on venous ulcer healing. *Australas J Dermatol* 1992; 33: 75–80 [CLIN S].
8. White RJ, Cooper R, Kingsley A. Wound colonization and infection: the role of topical antimicrobials *Br J Nurs* 2001; 10: 563–78 [LIT REV].
9. Madsen SM, Westh H, Danielsen L et al. Bacterial colonization and healing of venous leg ulcers. *APMIS* 1996; 104: 815–99 [CLIN S].
10. Holloway GA, Johansen, KH, Barnes, RW et al. Multicenter trial of cadexomer iodine to treat venous stasis ulcer. *West J Med* 1989; 151: 35–8 [RCT].

Guideline #3.4: Cellulitis (inflammation and infection of the skin and subcutaneous tissue most commonly due to streptococci or staphylococci) surrounding the venous ulcer should be treated with systemic gram-positive bactericidal antibiotics (Level II).

Principle: Edema fluid (plasma) neutralizes the fatty acids of sebum and inactivates the normal bactericidal properties of skin. This renders the skin and subcutaneous tissue susceptible to infection by streptococci and staphylococci.

Evidence:

1. Ricketts LR, Squire JR, Topley E et al. Human skin lipids with particular reference to the self-sterilizing power of the skin. *Clin Sci Mol Med* 1951; 10: 89–93 [EXP].
2. Baddour LM. Cellulitis syndromes: an update. *Int J Antimicrob Agent*s 2000; 14:113–6 [LIT REV].
3. Chiller K, Selkin BA, Murakawa GJ. Skin microflora and bacterial infections of the skin. *J Invest Dermatol Symp Proc* 2001; 6: 170–4 [LIT REV].
4. Guay DR. Treatment of bacterial skin and skin structure infections. *Expert Opin Pharmacother* 2003; 4: 1259–75 [LIT REV].
5. Edlich RF, Winters KL, Britt LD et al. Bacterial diseases of the skin. *J Long Term Eff Med Implants* 2005; 15: 499–510 [LIT REV].
6. Dall L, Peterson S, Simmons T et al. Rapid resolution of cellulites in patients managed with combination antibiotic and anti-inflammatory therapy. *Cutis* 2005; 75: 177–80 [RCT].

Guideline #3.5: Minimize the tissue level of bacteria, preferably to $\leq 10^5$ CFU/g of tissue, with no beta hemolytic streptococci in the venous ulcer before attempting surgical closure by skin graft, skin equivalent, pedicled, or free flap (Level II).

Principle: ''A wound containing contaminated foci with greater than 10^5 organisms per gram of tissue cannot be readily closed, as the incidence of wound infection that follows is 50–100%'' Tobin (1984).

Evidence:

1. Edlich RF, Rodeheaver GT, Thacker, JG et al. Management of soft tissue injury. *Clin Plast Surg* 1977; 4: 191–8 [LIT REV].
2. Liedberg NC, Reiss E, Artz CP. The effect of bacteria on the take of split thickness skin grafts in rabbits. *Ann Surg* 1955; 142: 92–6 [EXP].
3. Krizek TJ, Robson MC, Ko E. Bacterial growth and skin graft survival. *Surg Forum* 1968; 18: 518–9 [RCT].
4. Murphy RC, Robson MC, Heggers JP et al. The effect of contamination on musculocutaneous and random flaps. *J Surg Res* 1986; 41: 75–80 [EXP].
5. Tobin GR. Closure of contaminated wounds: Biologic and technical considerations. *Surg Clin North Am* 1984; 64: 639–52 [LIT REV].
6. Browne AC, Vearncombe M, Sibbald RG. High bacterial load in asymptomatic diabetic patients with neurotrophic ulcers retards wound healing after application of Dermagraft. *Ostomy/Wound Manage* 2001; 47: 44–9 [RCT].

GUIDELINES FOR *WOUND BED PREPARATION* IN THE TREATMENT OF VENOUS ULCERS

> Aspects of wound bed preparation are deliberately left out of this section because they are covered elsewhere. (Detailed discussions of infection control, dressings, and tissue engineering/growth factors are in Infection Control Guidelines, Dressings Guidelines, and Adjuvant Agents [Topical, Device, and Systemic] Guidelines.)

Preamble: Wound bed preparation is defined as the management of the wound to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures. The aim of wound bed preparation is to convert the molecular and cellular environment of a chronic wound to that of an acute healing wound. The principles of wound bed preparation have been enumerated:

- Schultz GS, Sibbald RG, Falanga V et al. Wound bed preparation: a systematic approach to wound management. *Wound Rep Reg* 2003; 11: 1s–23s.
- Sibbald RG, Williamson D, Orsted HL. Preparing the wound bed: debridement, bacterial balance, and moisture balance. *Ostomy/Wound Manage* 2000; 46: 14–35.

Guideline #4.1: Examination of the patient as a whole is important to evaluate and correct causes of tissue damage. This includes factors such as: (A) systemic diseases and medications, (B) nutrition, and (C) tissue perfusion and oxygenation (Level II).

Principle: (A) A general medical history and physical examination, including a medication record, will help in identifying and correcting systemic causes of impaired healing. The presence of a major illness or systemic disease and drug therapies such as immunosuppressive drugs and systemic steroids will interfere with wound healing by alterations in immune functioning, metabolism, inflammation, nutrition, and tissue perfusion. Autoimmune diseases such as rheumatoid arthritis, uncontrolled vasculitis, or pyoderma gangrenosum can all delay healing and may require systemic steroids or immunosuppressive agents before local wound healing can occur. Patients undergoing major surgery have a diminished wound-healing capacity as do chronic smokers. This information in addition to a detailed history of the wound itself is of benefit.

Evidence:

1. Lazarus GS, Cooper DM, Knighton DR et al. Definitions and guidelines for assessment of wounds and evaluation of healing. *Arch Dermatol* 1994; 130: 489–93 [STAT].
2. William DT, Harding K. Healing responses of skin and muscle in critical illness. *Crit Care Med* 2003; 31 (Suppl. 8): 547s–57s [LIT REV].
3. Beer HD, Fassler R, Werner S. Glucocorticoid-regulated gene expression during cutaneous wound repair. *Vitam Horm* 2000; 59: 217–39 [EXP].
4. Vaseliso M, Guaitro E. A comparative study of some anti-inflammatory drugs in wound healing in the rat. *Experientia* 1973; 29: 1250–1 [EXP].
5. Jorgensen LN, Kallehave F, Karlsmark T et al. Reduced collagen accumulation after major surgery. *Br J Surg* 1996; 83: 1591–4 [CLIN S].
6. Sorensen LT, Nielsen HB, Kharazini A et al. Effect of smoking and abstention on oxidative burst and reactivity of neutrophils and monocytes. *Surgery* 2004; 136: 1047–53 [RCT].
7. Mustoe T. Understanding chronic wounds: a unifying hypothesis on their pathogenesis and implications for therapy. *Am J Surg* 2004; 187 (5A): 65s–70s [LIT REV].

Principle: (B) Nutrition must be adequate to provide sufficient protein to support the growth of granulation tissue. Although most venous ulcer patients are ambulatory and not as nutritionally depleted as patients who require frequent or chronic hospitalization, nutritional support is required if an individual is undernourished.

Evidence:

1. Bourdel-Marchasson I, Barateau M, Rondeau V et al. A multicenter trial of the effects of oral nutritional supplementation in critically older inpatients. GAGE Group. Groupe Aquitain Gériatrique d'Evaluation. *Nutrition* 2000; 16: 1–5 [RCT].
2. Lansdown AB. Nutrition 2: a vital consideration in the management of skin wounds. *Br J Nurs* 2004; 13: 1199–210 [LIT REV].
3. Himes D. Protein-calorie malnutrition and involuntary weight loss: the role of aggressive nutritional intervention in wound healing. *Ostomy/Wound Manage* 1999; 45: 46–51, 54–5 [LIT REV].

Principle: (C) Wounds will heal in an environment that is adequately oxygenated. Oxygen delivery to a wound will be impaired if tissue perfusion is inadequate. Dehydration and factors that increase sympathetic tone such as cold, stress, or pain will all decrease tissue perfusion. Cigarette smoking decreases tissue oxygen by peripheral vasoconstriction. For optimal tissue perfusion, these factors must be eliminated or minimized.

Evidence:

1. Chang N, Goodson WH, Gottrup F et al. Direct measurement of wound and tissue oxygen tension in postoperative patients. *Ann Surg* 1983; 197: 470–8 [CLIN S].
2. Knighton DR, Halliday B, Hunt TK. Oxygen as an antibiotic. a comparison of the effects of inspired oxygen concentration and antibiotic administration on in vivo bacterial clearance. *Arch Surg* 1986; 121: 191–5 [EXP].
3. Hunt TK, Hopf HW. Wound healing and wound infection. What surgeons and anesthesiologists can do. *Surg Clin North Am* 1997; 77: 587–606 [LIT REV].
4. Jonsson K, Jensen JA, Goodson WH et al. Tissue oxygenation, anemia, and perfusion in relation to wound healing in surgical patients. *Ann Surg* 1991; 214: 605–13 [RCT].
5. Jensen JA, Goodson WH, Hopf HW et al. Cigarette smoking decreases tissue oxygen. *Arch Surg* 1991; 126: 1131–4 [RCT].
6. Hopf H, Hunt TK, West JM et al. Wound tissue oxygen tension predicts the risk of wound infection in surgical patients. *Arch Surg* 1997; 132: 997–1004 [CLIN S].
7. Gottrup F. Oxygen in wound healing and infection. *World J Surg* 2004; 28: 312–5 [LIT REV].
8. Hunt TK, Aslam RS. Oxygen 2002: wounds. *Undersea Hyperb Med* 2004; 31: 147–53 [LIT REV].

Guideline #4.2: Initial debridement is required to remove the obvious necrotic tissue, excessive bacterial burden, and cellular burden of dead and senescent cells. Maintenance debridement is needed to maintain the appearance and readiness of the wound bed for healing. The health care provider can choose from a number of debridement methods including sharp, enzymatic, mechanical, biological, or autolytic. More than one debridement method may be appropriate (Level I).

Principle: Necrotic tissue, excessive bacterial burden, senescent cells, and cellular debris can all inhibit wound healing. Sharp debridement is often the most advantageous. However, the method of debridement chosen may depend on the status of the wound, the capability of the health provider, the overall condition of the patient, and professional licensing restrictions. Excessive debridement can result in a reinstitution of the inflammatory process with a consequent influx of inflammatory cytokines.

Evidence:

1. Steed DL. Debridement. *Am J Surg* 2004; 187 (Suppl. 5A): 71s–4s [LIT REV].
2. Ayello EA, Cuddigan J. Debridement: controlling the necrotic/cellular burden. *Adv Skin Wound Care* 2004; 17: 66-75 [LIT REV].

3. Sieggreen MY, Maklebust J. Debridement: Choices and challenges. *Adv Wound Care* 1997; 10: 32–7 [LIT REV].
4. Bradley M, Cullum N, Sheldon T. The debridement of chronic wounds: a systematic review. *Health Technol Assess* 1999; 3(17 Part 1): 1–78 [STAT].
5. Sibbald RG, Williamson D, Orsted HL. Preparing the wound bed: debridement. bacterial balance, and moisture balance. *Ostomy/Wound Manage* 2000; 46: 14–35 [LIT REV].
6. Mosher BA, Cuddigan J, Thomas DR et al. Outcomes of 4 methods of debridement using a decision analysis methodology. *Adv Wound Care* 1999; 12: 81–8 [TECH].
7. Saap LJ, Falanga V. Debridement performance index and its correlation with complete closure of diabetic foot ulcers. *Wound Rep Reg* 2002; 10: 354–9 [RCT].
8. Davies CE, Turton G, Woolfrey G et al. Exploring debridement options for chronic venous leg ulcers. *Br J Nurs* 2005; 14: 393–7 [LIT REV].
9. Steed DL, Donohue D, Webster MW et al. Effect of extensive debridement on the healing of diabetic foot ulcers. Diabetic Ulcer Study Group. *J Am Coll Surg* 1996; 183: 61–4 [RCT].
10. Schmeller W, Gaber Y, Gehl HB. Shave therapy is a simple, effective treatment of persistent venous leg ulcers. *J Am Acad Dermatol* 1998; 39: 232–8 [CLIN S].
11. Falanga V. Wound bed preparation and the role of enzymes: a case for multiple actions of the therapeutic agents. *Wounds* 2002; 14: 47–57 [LIT REV].
12. Alvarez OM, Fernandez-Obregon A, Rogers RS et al. A prospective, randomized, comparative study of collagenase and papain-urea for pressure ulcer debridement. *Wounds* 2002; 14: 293–301 [RCT].
13. Rao DB, Sane PG, Georgiev EL. Collagenase in the treatment of dermal and decubitus ulcers. *J Am Geriatr Soc* 1975; 23: 22–30 [RCT].
14. Westerhof W, Van Ginkel CJ, Cohen EB et al. Prospective randomized study comparing the debriding effect of krill enzymes and a non-enzymatic treatment in venous leg ulcers. *Dermatologica* 1990; 181: 293–7 [RCT].
15. Mulder GD. Cost-effective managed care: gel versus wet-to-dry for debridement. *Ostomy/Wound Manage* 1995; 41: 68–74 [RCT].
16. Capasso VA, Munroe BH. The cost and efficacy of two wound treatments. *AORN J* 2003; 77: 995–7, 1000–4 [RETRO S].
17. Alvarez OM, Mertz PM, Eaglstein WH. The effect of occlusive dressings on collagen synthesis and re-epithelialization in superficial wounds. *J Surg Res* 1983; 35: 142–8 [EXP].
18. Limova M. Evaluation of two calcium alginate dressings in the management of venous ulcers. *Ostomy/Wound Manage* 2003; 49:26–33 [RCT].
19. Koksal C, Bozkurt AK. Combination of hydrocolloid dressing and medical compression stockings versus Unna's boot for the treatment of venous leg ulcers. *Swiss Med Wkly* 2003; 133: 364–8 [RCT].

Guideline #4.3: Wounds should be cleansed initially and at each dressing change using a neutral, nonirritating, nontoxic solution. Routine wound cleansing should be accomplished with a minimum of chemical and/or mechanical trauma (Level III).

Principle: Irrigating and cleansing the wound removes loose impediments to wound healing. Sterile saline or water is usually recommended. Tap water should only be used if the water source is reliably clean. Experimental data suggest that a nontoxic surfactant may be useful as may fluid delivered by increased intermittent pressure.

Evidence:

1. Rodeheaver GT. Wound cleansing, wound irrigation, wound disinfection. In: Krasner D, Kane D, editors. *Chronic Wound Care: A Clinical Source Book for Healthcare Professionals*. Wayne, PA: Health Management Publications, Inc., 1997: 97–108 [LIT REV].
2. Morris EJ, Dowlen S, Cullen B. Early clinical experience with topical collagen in vascular wound care. *J Wound Ostomy Continence Nurs* 1994; 21: 247–50 [CLIN S].
3. Rodeheaver GT, Kurtz L, Kircher BJ et al. Pluronic F-68: a promising new skin wound cleanser. *Ann Emerg Med* 1980; 9: 572–6 [EXP].
4. Hamer MI, Robson MC, Krizek TJ et al. Quantitative bacterial analysis of comparative wound irrigations. *Ann Surg* 1975; 181: 819–22 [EXP].

Guideline #4.4: There should be an ongoing and consistent documentation of wound history, recurrence, and characteristics (location, size, base, exudates, condition of the surrounding skin, staging, and pain) to evaluate wound bed preparation. The rate of wound healing should be evaluated to determine whether treatment is optimal (Level I).

Principle: Ongoing evaluations of wound bed preparation are necessary because if the ulcer is not healing at the expected rate, interventions for wound bed preparation need to be reassessed. The longer the duration of the ulcer, the more difficult it is to heal. If an ulcer is recurrent, patient education or issues of prevention and long-term maintenance need to be reassessed.

Evidence:

1. Lazarus GS, Cooper DM, Knighton DR et al. Definitions and guidelines for assessment of wounds and evaluation of healing. *Arch Dermatol* 1994; 130: 489–93 [STAT].
2. Saap LJ, Falanga V. Debridement performance index and its correlation with complete closure of diabetic foot ulcers. *Wound Rep Reg* 2002; 10: 354–9 [RCT].
3. Krasner D. Wound healing scale, version 1.0: a proposal. *Adv Wound Care* 1997; 10: 82–5 [TECH].
4. Porter JM, Moneta GL, International Consensus Committee on Chronic Venous Disease. Reporting standards on venous disease: an update. *J Vasc Dis* 1995; 21: 635–45 [STAT].
5. Beebe HG, Bergan JJ, Bergqvist D et al. Classification and grading of chronic venous disease in the lower limbs: a consensus statement. *Eur J Vasc Endovasc Surg* 1996; 12: 487–92 [STAT].
6. Ratliff CR, Rodeheaver GT. Use of the PUSH tool to measure venous ulcer healing. *Ostomy/Wound Manage* 2005; 51: 58–63 [CLIN S].
7. Kantor J, Margolis DJ. A multicentre study of percentage change in venous leg ulcer area as a prognostic index of healing at 24 weeks. *Br J Dermatol* 2000; 142: 960–4 [STAT].

8. van Rijswijk L, Multi-Center Leg Ulcer Study Group. Full-thickness leg ulcers: patient demographics and predictors of healing. *J Fam Prac* 1993; 36: 625–32 [RCT].

GUIDELINES FOR *DRESSINGS* IN THE TREATMENT OF VENOUS ULCERS

Preamble: There is a plethora of choices for topical treatment of venous ulcers. Many dressings now combine wound bed preparation, i.e., debridement and/or antimicrobial activity, with moisture control. Guidelines are necessary to help the clinician make decisions regarding the value and best use of these advanced wound care products. Most dressings will be used in combination with compression systems (see Compression Guidelines).

Guideline # 5.1: Use a dressing that will maintain a moist wound-healing environment (Level I).

Principle: A moist wound environment physiologically favors cell migration and matrix formation while accelerating healing of wounds by promoting autolytic debridement. Moist wound healing also reduces pain. Dry dressings, except over intact skin, are considered injurious and can cause desiccation of the wound.

Evidence:

1. Winter GD, Scales JT. Effect of air drying and dressings on the surface of a wound. *Nature* 1963; 197: 91–2 [EXP].
2. Breuing K, Eriksson E, Liu P et al. Healing of partial thickness porcine skin wounds in a liquid environment. *J Surg Res* 1992; 52: 50–8 [EXP].
3. Svensjo T, Pomahac B, Yao F et al. Accelerated healing of full-thickness skin wounds in a wet environment. *Plast Reconstr Surg* 2000; 106: 602–12 [EXP].
4. Vranckx JJ, Slama J, Preuss S et al. Wet wound healing. *Plast Reconstr Surg* 2002; 110: 1680–7 [CLIN S].
5. Margolis DJ, Cohen JH. Management of chronic venous ulcers: a literature-guided approach. *Clin Dermatol* 1994; 12: 19–26 [LIT REV].
6. Stacey MC, Jopp-McKay AG, Rashid P et al. The influence of dressings on venous ulcer healing—a randomized trial. *Eur J Vasc Endovasc Surg* 1997; 13: 174–9 [RCT].
7. Briggs M, Nelson EA. Topical agents or dressings for pain in venous leg ulcers. *The Cochrane Database of Systematic Reviews* 2003 Issue 1. CD001177. The Cochrane Collaboration. John Wiley & Sons Ltd. [STAT].
8. Ovington LG. Hanging wet-to-dry dressings out to dry. *Home Healthcare Nurse* 2001; 19: 477–84 [LIT REV].
9. Kerstein MD, Gemmen E, vanRijswijk L, Lyder CH, Golden K, Harrington C. Cost and cost effectiveness of venous and pressure ulcer protocols of care. *Dis Manage Health Outcomes* 2001; 9: 631–6 [STAT].
10. Friedman SJ, Su DS. Management of leg ulcers with hydrocolloid occlusive dressing. *Arch Dermatol* 1984; 120: 1329–36 [RCT].

Guideline #5.2: Use clinical judgment to select a wound dressing that facilitates continued moisture (Level I).

Principle: Wet-to-dry dressings are not considered continuously moist. Continuously moist saline gauze dressings are as effective as other types of moist wound healing in terms of healing rate, although they may have other drawbacks such as maceration of the peri-ulcer skin, practicality of use, and cost effectiveness. It can also be very difficult, practically, to keep gauze dressings continuously moist.

Evidence:

1. Bouza C, Munoz A, Amate JM. Efficacy of modern dressings in the treatment of leg ulcers: a systematic review. *Wound Rep Reg* 2005; 3: 218–29 [LIT REV].
2. Geronemus RG, Robins P. The effect of two dressings on epidermal wound healing. *J Derm Surg Oncol* 1982; 8: 850–2 [EXP].
3. Blair SD, Jarvis P, Salmon M et al. Clinical trial of calcium alginate haemostatic swabs. *Br J Surg* 1990; 77: 568–70 [RCT].
4. Arnold TE, Stanley JC, Fellows WP et al. Prospective multicenter study managing lower-extremity venous ulcers. *Ann Vasc Surg* 1994; 8: 356–62 [RCT].
5. Sayag J, Meaume S, Bohbot S. Healing properties of calcium alginate dressings. *J Wound Care* 1996; 5: 357–62 [RCT].
6. Bradley M, Cullum N, Nelson EA et al. Systematic reviews of wound care management. (2) Dressings and topical agents used in the healing of chronic wounds. *Health Technol Assess* 1999; 3: 1–35 [STAT].
7. Charles H, Callicot C, Mathurin D et al. Randomized comparative study of three primary dressings for the treatment of venous ulcers. *Br J Commun Nurs* 2002; 7(Suppl. 6): 48–54 [RCT].
8. Ovington LG. Hanging wet-to-dry dressings out to dry. *Home Healthcare Nurse* 2001; 19: 477–84 [LIT REV].

Guideline # 5.3: Select a dressing that will manage the wound exudate and protect the peri-ulcer skin (Level I).

Principle: Peri-wound maceration and continuous contact with wound exudate can enlarge the wound and impede healing.

Evidence:

1. Bucalo B, Eaglstein WH, Falanga V. Inhibition of cell proliferation by chronic wound fluid. *Wound Rep Reg* 1993; 1: 181–6 [EXP].
2. Trengove NJ, Stacey MC, Mac Auley S et al. Analysis of the acute and chronic wound environments: the role of proteases and their inhibitors. *Wound Rep Reg* 1999; 7: 442–52 [EXP].
3. Yager DR, Zhang LY, Liang HX et al. Wound fluids from human pressure ulcers contain elevated matrix metalloproteinase levels and activity compared to surgical wound fluids. *J Invest Derm* 1996; 107: 743–8 [EXP].
4. Tarlton JF, Bailey AJ, Crawford E et al. Prognostic value of markers of collagen remodeling in venous ulcers. *Wound Rep Reg* 1999; 7: 347–55 [EXP].
5. Sayag J, Meaume S, Bohbot S. Healing properties of calcium alginate dressings. *J Wound Care* 1996; 5: 357–62 [RCT].

6. Limova M. Evaluation of two calcium alginate dressings in the management of venous ulcers. *Ostomy/Wound Manage* 2003; 49: 26–33 [RCT].
7. Hansson C. The effects of cadexomer iodine paste in the treatment of venous leg ulcers compared with hydrocolloid dressing and paraffin gauze dressing. *Int J Dermatol* 1998; 37: 390–6 [RCT].
8. Gallenkemper G, Rabe E, Bauer R. Contact sensitization in chronic venous insufficiency: modern wound dressings. *Contact Dermatitis* 1998; 38: 274–8 [LIT REV].

Guideline #5.4: Select a dressing that stays in place, minimizes shear and friction, and does not cause additional tissue damage (Level II).

Principle: Wound location, peri-wound skin quality, and patient activity can all affect the choice of dressing. The use of compression systems for venous ulcers alleviates the need for adhesive to keep the primary dressing in place. However, additional tissue damage may result if the dressing causes increased pressure on the wound or damages adjacent tissue. Venous ulcer patients are particularly susceptible to contact dermatitis related to topical therapies.

Evidence:

1. Sasseville D, Tennstedt D, Lachapelle JM. Allergic contact dermatitis from hydrocolloid dressings. *Am J Contact Dermat* 1997; 8: 236–8 [CLIN S].
2. Dooms-Goosen A, Degreef H, Parijs M et al. A retrospective study of Patch test results from 163 patients with stasis dermatitis or leg ulcers: I. Discussion of the Patch test results and the sensitization indices and determination of the relevancy of positive reactions. *Dermatologica* 1979; 159: 93–100 [RETRO S].
3. Fraki JE, Peltonen L, Hopsu-Havu VK. Allergy to various components of topical preparations in stasis dermatitis and leg ulcer. *Contact Dermatitis* 1979; 5: 97–100 [CLIN S].
4. Kulozik M, Powell SM, Cherry G et al. Contact sensitivity in community-based leg ulcer patients. *Clin Exp Dermatol*. 1988; 13: 82–4 [CLIN S].
5. Hess CT. Identifying and managing venous dermatitis. *Adv Skin Wound Care* 2005; 18: 242–3 [LIT REV].
6. Gallenkemper G, Rabe E, Bauer R. Contact sensitization in chronic venous Insufficiency: modern wound dressings. *Contact Dermatitis* 1998; 38: 274–8 [LIT REV].

Guideline #5.5: Select a dressing that is cost effective and appropriate to the setting and the provider (Level I).

Principle: Because of their low unit cost, moist saline gauze dressings are often viewed as the least expensive and, therefore, most cost-effective dressing. However, as pointed out in Guideline #5.2, it is very difficult to keep a gauze dressing continuously moist. When determining cost effectiveness, it is important to take into consideration health care provider time, ease of use, and healing rate, as well as the unit cost of the dressing.

Evidence:

1. Ohlsson P, Larsson K, Linkholm C et al. A cost-effectiveness study of leg ulcer treatment in primary care. *Scand J Prim Health Care* 1994; 12: 295–9 [RCT].
2. Harding KG, Price P, Robinson B et al. Cost and dressing evaluation of hydrofiber and alginate dressings in the management of community-based patients with chronic leg ulceration. *Wounds* 2001; 13: 229–36 [RCT].
3. Schonfeld WH, Villa KF, Fastenau JM et al. An economic assessment of APLIGRAF (Graftskin) for the treatment of hard-to-heal venous leg ulcers. *Wound Rep Reg* 2000; 8: 251–7 [RCT].
4. Vanschendt W, Sibbald RG, Eager CA. Comparing a foam composite to a hydrocellular foam dressing in the management of venous leg ulcers: a controlled clinical study. *Ostomy/Wound Manage* 2004; 50: 42–55 [RCT].
5. Ovington LG. Hanging wet-to-dry dressings out to dry. *Home Healthcare Nurse* 2001; 19: 477–84 [LIT REV].
6. Kerstein MD, Gemmen E, vanRijswijk et al. Cost and cost effectiveness of venous and pressure ulcer protocols of care. *Dis Manage Health Outcomes* 2001; 9: 631–6 [STAT].

Guideline #5.6: Selectively use adjuvant agents (topical, device, and/or systemic) after evaluating individual patient/ulcer characteristics and when there is a lack of healing progress in response to more traditional therapies. (Detailed discussions of these alternatives are in Adjuvant Agents [Topical, Device, Systemic] Guidelines; Level I.)

Principle: Emerging therapies through recombinant technologies and cell-based devices may offer benefit and increase healing in selected patients or difficult wounds. These therapies are quite diverse and are discussed in detail in the Adjuvant Agents Guidelines.

Evidence: Evidence references are detailed in the Adjuvant Agents (Topical, Device, Systemic) Guidelines.

GUIDELINES FOR *SURGERY* IN THE TREATMENT OF VENOUS ULCERS

Preamble: The mainstays of moist wound dressings and a compression system are not successful in healing all venous ulcers. Also, they do not fully address the etiology of increased ambulatory venous pressure. Over the years, multiple surgical procedures have been attempted to treat venous ulcers with varying degrees of success. True randomized clinical trials comparing operative techniques are rare in the literature, but data are available supporting surgery in selected patients. These data include a cross-over study (DePalma RG, Kowallek DL. Venous ulceration: a cross-over study from nonoperative to operative treatment. *J Vasc Surg* 1996; 24: 788–92).

Guideline #6.1: Skin grafting of a venous ulcer, without attention to the underlying venous disease, is not a long-term solution and is prone to recurrent leg ulceration (Level I).

Principle: Closing the venous ulcer with an autologous skin graft (pinch graft, split-thickness graft, meshed graft, full-thickness graft) may provide a short-term goal of wound closure but does not address the increased ambulatory venous pressure (venous hypertension) that is the underlying cause of the ulcer.

Evidence:

1. Jones JE, Nelson EA. Skin grafting for venous ulcers. *The Cochrane Database of Systematic Reviews. Issue 1*. The Cochrane Collaboration: John Wiley & Sons Ltd., 2005 [STAT].
2. Turczynski R, Tarpila E. Treatment of leg ulcers with split skin grafts: early and late results. *Scand J Plast Reconstr Hand Surg* 1999; 33: 301–5 [CLIN S].
3. Poskitt KR, James AH, Lloyd-Davies, ER et al. Pinch skin grafting or porcine dermis in venous ulcers: a randomized trial. *Br Med J (Clin Res Ed)* 1987; 294: 674–6 [RCT].
4. Kirsner RJ, Mata SM, Falanga V et al. Split-thickness skin grafting of leg ulcers. *Dermatol Surg* 1995; 21: 701–3 [CLIN S].

Guideline #6.2: Subfascial endoscopic perforator surgery (SEPS) is the procedure of choice when it is desirable to address the underlying venous pathologic etiology of the ulcer by preventing backflow from the deep to the superficial venous system. To achieve the greatest effectiveness when using this procedure, care must be taken to divide all visible perforators. The procedure is not effective if the patient has severe deep venous disease with either deep reflux or obstruction. The SEPS procedure, with or without skin grafting or use of a bilayered artificial skin, has a lower complication rate, and compares favorably with the more formidable open procedure in terms of ulcer healing and recurrence (Level I).

Principle: Interruption of incompetent perforating vessels will aid in decreasing elevated ambulatory venous pressure in the leg.

Evidence:

1. Pierik EG, vanUrk H, Hop WC et al. 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 [RCT].
2. Warburg FE, Danielsen L, Madsen SM et al. Vein surgery with or without skin grafting versus conservative treatment for leg ulcers. A randomized prospective study. *Acta Derm Venereol* 1994; 74: 307–9 [RCT].
3. Gloviczki P, Bergan JJ, Rhodes JM et al. Mid-term results of endoscopic perforator vein interruption for chronic venous insufficiency: lessons learned from the North American subfascial endoscopic perforator surgery registry. The North American Study Group. *J Vasc Surg* 1999; 489–502 [STAT].
4. Sybrandy JE, vanGent WB, Pierik EG et al. 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 [RCT].
5. Kalra M, Gloviczki P. Surgical treatment of venous ulcers: Role of subfascial endoscopic perforator vein ligation. *Surg Clin North Am* 2003; 83: 671–705 [LIT REV].
6. Baron HC, Wayne MG, Santiago CA et al. Endoscopic subfascial perforator vein surgery for patients with severe, chronic venous insufficiency. *Vasc Endovasc Surg* 2004; 38: 439–42 [CLIN S].
7. Mendes RR, Marston WA, Farner MA et al. Treatment of superficial and perforator venous incompetence without deep vein insufficiency: is routine perforator ligation necessary? *J Vasc Surg* 2003; 38: 891–5 [CLIN S].

Guideline #6.3: Less extensive surgery on the venous system such as superficial venous ablation, endovenous laser ablation, or valvuloplasty, especially when combined with compression therapy, can be useful in decreasing the recurrence of venous ulcers (Level I).

Principle: Procedures that are less extensive than deep ligation of multiple perforating veins can help to decrease venous hypertension when combined with an adequate compression system.

Evidence:

1. Barwell JR, Davies CE, Deacon J et al. Comparison of surgery and compression with compression alone in chronic venous ulceration (ESCHAR study): randomized controlled trial. *Lancet* 2004; 363: 1854–9 [RCT].
2. Gobel MS, Barwell JR, Earnshaw JJ et al. Randomized clinical trial of compression plus surgery versus compression alone in chronic venous ulceration (ESCHAR study)—hemodynamic and anatomical changes. *Br J Surg* 2005; 92: 291–7 [RCT].
3. Zamboni P, Cisno C, Marchetti F et al. Minimally invasive surgical management of primary venous ulcers vs. compression treatment: a randomized clinical trial. *Eur J Vasc Endovasc Surg* 2003; 25: 313–8 [RCT].
4. 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 [STAT].
5. Perrin M, Hiltbrand B, Bayon JM. Results of valvuloplasty in patients presenting deep vein insufficiency and recurring ulceration. *Ann Vasc Surg* 1999; 13: 524–32 [CLIN S].

Guideline #6.4: Free flap transfer with microvascular anastomoses can benefit recalcitrant venous ulcers with severe lipodermatosclerosis by allowing wide excision of diseased tissue and providing uninjured venous valves in the transferred tissue (Level II).

Principle: Composite tissue from a nondiseased region of the body can bring abundant tissue with its own microvasculature to an area of injury.

Evidence:

1. Dunn RM, Fudam GM, Walton RL et al. Free flap valvular transplantation for refractory venous ulceration. *J Vasc Surg* 1994; 19: 525–31 [CLIN S].
2. Kumins NH, Weinzweig N, Schuler JJ. Free tissue transfer provides durable treatment for large nonhealing venous ulcers. *J Vasc Surg* 2000; 32: 848–54 [CLIN S].
3. Aharinejad S, Dunn RM, Nourani F et al. Morphological and clinical aspects of scapular fasciocutaneous free flap transfer for treatment of venous insufficiency in the lower extremity. *Clin Anat* 1998; 11: 38–46 [PATH S].

4. Weinzweig N, Schuler J. Free tissue transfer in treatment of the recalcitrant chronic venous ulcer. *Ann Plast Surg* 1997; 38: 611–9 [CLIN S].
5. Isenberg JS. Additional follow-up with microvascular transfer in the treatment of chronic venous stasis ulcers. *J Reconstr Microsurg* 2001; 17: 603–5 [RETRO S].

GUIDELINES FOR THE *USE OF ADJUVANT AGENTS (TOPICAL, DEVICE, AND SYSTEMIC)* IN THE TREATMENT OF VENOUS ULCERS

Preamble: Many agents have been suggested for use as adjuvants to moist wound-healing dressings and compression therapy in the treatment of venous ulcers. These adjuvant agents can be divided into topical agents to be applied to the ulcer, devices aimed at accelerating ulcer healing, and systemic drugs to treat the patient. Several of these agents have enough evidence to allow guidelines regarding their use to be developed.

TOPICAL AGENTS

Guideline #7a.1: Cytokine growth factors have yet to be shown to demonstrate sufficient statistically significant results of effectiveness to recommend any of them for treatment of venous ulcers, although isolated reports suggest their potential usefulness (Level I).

Principle: Cytokine growth factors are messengers/mediators of the wound-healing scheme. They have been shown to be deficient or trapped in chronic wounds, so theoretically they could be useful for treatment of venous ulcers, and several authors have reported positive results in small series.

Evidence:

1. Stacey MC, Mata SD, Trengove NJ et al. Randomized double-blind placebo-controlled trial of topical autologous platelet lysate in venous ulcer healing. *Eur J Vasc Endovasc Surg* 2000; 20: 296–301 [RCT].
2. Coerper S, Koveker G, Flesch I et al. Ulcus cruris venosum: surgical debridement, antibiotic therapy, and stimulation with thrombocytic growth factors. *Langenbacks Arch Chir* 1995; 380: 102–7 [CLIN S].
3. Reutter H, Bort S, Jung MF et al. Questionable effectiveness of autologous platelet growth factors (PDWHF) in the treatment of venous ulcers of the leg. *Hartarzt* 1999; 50: 859–65 [RCT].
4. DaCosta RM, Ribeiro J, Aniceto C et al. Randomized, double-blind, placebo-controlled, dose-ranging study of granulocyte-macrophage colony-stimulating factor in patients with chronic venous ulcers. *Wound Rep Reg* 1999; 7: 17–25 [RCT].
5. Jashke E, Zabernigg A, Gattringer C. Recombinant human granulocyte-macrophage colony-stimulating factor applied locally in low doses enhances healing and prevents recurrence of chronic venous ulcers. *Int J Dermatol* 1999: 38: 380–6 [CLIN S].
6. Falanga V, Eaglstein WH, Bucalo B et al. Topical use of human recombinant epidermal growth factor (h-EGF) in venous ulcers. *J Dermatol Surg Oncol* 1992; 18: 604–6 [RCT].
7. Robson MC, Phillips LG, Cooper DM et al. The safety and effect of transforming growth factor-B2 for treatment of venous stasis ulcers. *Wound Rep Reg* 1995; 3: 157–67 [RCT].
8. Robson MC, Phillips TJ, Falanga V et al. Randomized trial of topically applied repifermin (recombinant keratinocyte growth factor-2) to accelerate healing in venous ulcers. *Wound Rep Reg* 2001; 9: 347–52 [RCT].
9. Robson MC, Hanfnt J, Garner W et al. Healing of chronic venous ulcers is not enhanced by the addition of topical repifermin (KGF-2) to standardized care. *J Appl Res* 2004; 4: 302–11 [RCT].
10. Pierce GF, Tarpley JE, Tseng J et al. Detection of increased levels of PDGF-AArh in healing wounds treated with recombinant PDGF-BB, and absence of PDGF in chronic nonhealing wounds. *JCI* 1995; 96: 1336–50 [RCT].
11. Cooper DM, Yu EZ, Hennessey P et al. Determination of endogenous cytokines in chronic wounds. *Ann Surg* 1994; 219: 688–92 [EXP].
12. Falanga V, Eaglstein WH. The "trap" hypothesis of venous stasis ulcers. *Lancet* 1993; 341: 1006–8 [EXP].

Guideline #7a.2: Topical application of oxygen-derived free radical scavengers have been reported to be beneficial for treatment of venous ulcers, as has a topical fibrinolytic agent. Neither of these modalities have sufficient data to recommend their use (Level I).

Principle: Ischemia–reperfusion injury mediated by oxygen-derived free radicals has been suggested to play a role in the etiology of venous ulcers. Fibrin deposition is also an important pathogenic component of venous ulceration. Therefore, agents to decrease or abrogate these effects could theoretically be useful treatments.

Evidence:

1. Salim AS. Role of sulhydryl-containing agents in the management of venous (varicose) ulceration. A new approach. *Clin Exp Dermatol* 1992; 17: 427–32 [RCT].
2. Salim AS. The role of oxygen-derived free radicals in the management of venous (varicose) ulceration: a new approach. *World J Surg* 1991; 15: 264–9 [RCT].
3. Falanga V, Carson P, Greenberg A et al. Topically applied recombinant tissue plasminogen activator for the treatment of venous ulcers. Preliminary report. *Dermatol Surg* 1996; 22: 643–4 [RCT].

DEVICES

Guideline #7b.1: There is evidence that a bilayered artificial skin (biologically active dressing), used in conjunction with compression bandaging, increases the chance of healing a venous ulcer compared with compression and a simple dressing (Level I).

Principle: Various skin substitutes or biologically active dressings are emerging that provide temporary wound closure and serve as a source of stimuli (e.g., growth factors) for healing of venous ulcers.

Evidence:

1. Jones JE, Nelson EA. Skin grafting for venous ulcers. *The Cochrane Database of Systematic Reviews Issue 1*. The Cochrane Collaboration: John Wiley & Sons Ltd., 2005 [STAT].
2. Falanga V, Margolis D, Alvarez O et al. Rapid healing of venous ulcers and lack of clinical rejection with an allogeneic cultured human skin equivalent. Human Skin Equivalent Investigators Group. *Arch Dermatol* 1998; 134: 293–300 [RCT].
3. Atillasoy E. The safety and efficacy of Graftskin (Apligraf) in the treatment of venous leg ulcers: a multicenter, randomized, controlled clinical trial. *Wounds* 2000; 12 (Suppl. A): 20A–6A [RCT].
4. Omar AA, Mavor AI, Jones AM et al. Treatment of venous ulcers with Dermagraft. *Eur J Vasc Endovasc Surg* 2004; 27: 666–72 [RCT].
5. Brem H, Balledux J, Sukkarieh T et al. Healing of venous ulcers of long duration with a bilayered living skin substitute: results from a general surgery and dermatology department. *Dermatol Surg* 2001; 27: 915–9 [CLIN S].
6. Snyder RJ, Simonson DA. Cadaveric allograft as adjunct therapy for nonhealing ulcers. *J Foot Ankle Surg* 1999; 38: 93–101 [RETRO S].

Guideline #7b.2: Cultured epithelial autografts or allografts have not been demonstrated to improve stable healing of venous ulcers (Level I).

Principle: Although cultured epithelial autografts (CEA) have been useful in thermal burns, they do not appear to be durable enough to be sustained on venous leg ulcers.

Evidence:

1. Teepe RG, Roseeuw DI, Hermans J et al. Randomized trial comparing cryopreserved cultured epidermal allografts with hydrocolloid dressings in healing chronic venous ulcers. *J Am Acad Dermatol* 1993; 29: 982–8 [RCT].
2. Lindgren C, Marcusson JA, Toftgard R. Treatment of venous leg ulcers with cryopreserved cultured allogeneic keratinocytes: a prospective open controlled study. *Br J Dermatol* 1998; 139: 271–5 [RCT].
3. Limova M, Mauro T. Treatment of leg ulcers with cultured epithelial autografts. Clinical study and case reports. *Ostomy/Wound Manage* 1995; 41: 48–60 [CLIN S].
4. Leigh IM, Purkis PE, Navsaria HA et al. Treatment of chronic venous ulcers with sheets of cultured allogeneic keratinocytes. *Br J Dermatol* 1987; 117: 591–7 [CLIN S].

Guideline #7b.3: Electrical stimulation may be useful in reducing the size of venous leg ulcers (Level I).

Principle: Various methods of electrical stimulation have been reported to improve wound healing in many settings. Not enough data exist to determine whether the electrical stimulus should be high voltage, low voltage, or pulsed and whether AC or DC current is superior.

Evidence:

1. Franek A, Polak A, Kucharzewski M. Modern application of high voltage stimulation for enhanced healing of venous crural ulceration. *Med Eng Phys* 2000; 22: 647–55 [RCT].
2. Houghton PE, Kincaid CB, Lovell M et al. Effect of electrical stimulation on chronic leg ulcer size and appearance. *Phys Ther* 2003; 83: 17–28 [RCT].
3. Stiller MJ, Pak GH, Shupack JL et al. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind placebo-controlled trial. *Br J Dermatol* 1992; 127: 147–54 [RCT].

Guideline #7b.4: Negative pressure wound therapy may be useful prior to a skin graft/flap by helping promote the development of granulation tissue in the wound base, or postoperatively by preventing shearing and removing exudates. However, its reported experience in venous ulcers is limited (Level II).

Principle: Negative pressure wound therapy applies negative pressure to help remove fluid, assist in granulation tissue formation, decrease wound size, and help promote skin graft take.

Evidence:

1. Moisidis E, Heath T, Boorer et al. A prospective, blinded, randomized, controlled clinical trial of topical negative pressure use in skin grafting. *Plast Reconstr Surg* 2004; 114: 917–22 [RCT].
2. Carson SN, Overall K, Lee-Jahshan S et al. Vacuum-assisted closure used for healing chronic wounds and skin grafts in the lower extremities. *Ostomy Wound Manage* 2004; 50: 52–8 [RETRO S].
3. Morykwas MJ, Argenta LC, Shelton-Brown EI et al. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. *Ann Plast Surg* 1997; 38: 553–62 [EXP].
4. Joseph E, Hamori CA, Bergman S et al. A prospective randomized trial of vacuum-assisted closure versus standard therapy of chronic nonhealing wounds. *Wounds* 2000; 12: 60–7 [RCT].

Guideline #7b.5: Laser therapy, phototherapy, and ultrasound therapy have *not* been shown statistically to improve venous ulcer healing (Level I).

Principle: There are theoretical reasons and preclinical studies suggesting that modalities such as laser therapy, phototherapy, and ultrasound therapy might be useful in the treatment of venous ulcers. Available evidence does not support their use.

Evidence:

1. Flemming KA, Cullum NA, Nelson EA. A systematic review of laser therapy for venous leg ulcers. *J Wound Care* 1999; 8: 111–4 [STAT].
2. Lagan KM, McKenna T, Witherow A et al. Low-intensity laser therapy/combined phototherapy in the management of chronic venous ulceration: a placebo-controlled study. *J Clin Laser Med Surg* 2002; 20: 109–16 [RCT].

3. Kopera D, Kokol R, Berger C et al. Does the use of low-level laser influence wound healing in chronic venous leg ulcers? *J Wound Care* 2005; 14: 391–4 [RCT].
4. Johannsen G, Gam AN, Karlsmark T. Ultrasound therapy in chronic leg ulceration: a meta-analysis. *Wound Rep Reg* 1998; 6: 121–6 [STAT].
5. Cullum N, Nelson EA, Flemming K et al. Systematic reviews of wound care management: (5) beds; (6) compression; (7) laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy. *Health Technol Assess* 2001; 5: 1–221 [STAT].

Guideline #7b.6: Sclerotherapy may be useful as an adjunct to compression therapy in the treatment of venous ulcers (Level III).

Principle: Sclerosing superficial veins may be similar to surgical superficial vein ablation, which, when used with an adequate compression system, may improve ulcer treatment.

Evidence:

1. Queral LA, Criado FJ, Lilly MP et al. The role of sclerotherapy as an adjunct to Unna's boot for treating venous ulcers: a prospective study. *J Vasc Surg* 1990; 11: 572–5 [RCT].

SYSTEMIC AGENTS

Guideline #7c.1: Pentoxifylline used in conjunction with compression therapy improves healing of venous ulcers (Level I).

Principle: Improvement to the microcirculation of the leg should theoretically aid the healing processes of venous ulcers.

Evidence:

1. Jull A, Waters J, Arroll B. Pentoxifylline for treating venous leg ulcers. *The Cochrane Database of Systematic Reviews. Issue 1*. The Cochrane Collaboration: John Wiley & Sons Ltd., 2002 [STAT].
2. 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; 7: 208–13 [RCT].
3. DeSanctis MT, Belcaro G, Cesarone MR et al. Treatment of venous ulcers with pentoxifylline: a 12-month, double-blind, placebo controlled trial. Microcirculation and healing. *Angiology* 2002; 53 (Suppl. 1): s49–51 [RCT].
4. Belcaro G, Cesarone MR, Nicolaides AN et al. Treatment of venous ulcers with pentoxifylline: a 6-month randomized, double-blind, placebo controlled trial. *Angiology* 2002; 53 (Suppl. 1): s45–7 [RCT].
5. Colgan MP, Dormandy JA, Jones PW et al. Oxpentifylline treatment of venous ulcers of the leg. *Br Med J* 300; 972–5 [RCT].
6. Barbarino C. Pentoxifylline in the treatment of venous leg ulcers. *Curr Med Res Opin* 1992; 12: 547–51 [RCT].
7. Dale JJ, Ruckley CV, Harper DR et al. Randomized, double-blind placebo controlled trial of pentoxifylline in the treatment of venous leg ulcers. *Br Med J* 1999; 319: 875–8 [RCT].

Guideline #7c.2: The role of eicosanoids (prostaglandins) or prostaglandin antagonists in the treatment of venous ulcers lacks sufficient data to allow a recommendation (Level II).

Principle: Vasodilating and antiplatelet sticking effects of certain eicosanoids such as PGE or PGI could theoretically improve venous insufficiency and minimize ulceration.

Evidence:

1. Rudofsky G. Intravenous prostaglandin E1 in the treatment of venous ulcers: a double-blind, placebo-controlled trial. *Vasa Suppl* 1989; 281: 39–43 [RCT].
2. Beitner H, Hammar H, Olsson AG et al. Prostaglandin E1 treatment of leg ulcers caused by venous or arterial incompetence. *Acta Derm Venereol* 1980; 60: 425–30 [RCT].
3. Ibbotson SH, Layton AM, Davies JA et al. The effect of aspirin on haemostatic activity in the treatment of chronic venous leg ulceration. *Br J Dermatol* 1995; 132: 422–6 [RCT].

Guideline #7c.3: Oral treatment with micronized purified flavonoid fraction (MPFF) may be a useful adjunct to conventional compression therapy in the treatment of leg ulcers (Level I).

Principle: Agents that inhibit synthesis of prostaglandins and free oxygen radicals, decrease microvascular leakage, and inhibit leukocyte trapping and activation should theoretically aid in the healing of venous ulcers.

Evidence:

1. 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; 30: 198–208 [STAT].
2. Gilhou JJ, Ferrier F, Debure C et al. Benefit of a 2-month treatment with a micronized, purified flavonoidic fraction on venous ulcer healing. A randomized, double-blind, controlled versus placebo trial. *Int J Microcirc Clin Exp* 1997; 17 (Suppl. 1): 21–6 [RCT].
3. Glinski W, Chodynicka B, Roszkiewicz J. The beneficial augmentative effect of micronized purified flavonoid fraction on the healing of leg ulcers. An open multicenter, controlled randomized study. *Phlebology* 1994; 14: 151–7 [RCT].
4. Bergan JJ, Schmid-Schonbein GW, Takase S. Therapeutic approach to chronic venous insufficiency and its complications: place of Daflon 500 mg. *Angiology* 2001; 52 (Suppl. 1): s43–7 [LIT REV].
5. Ramelet AA. Clinical benefits of Daflon 500 mg in the most severe stages of chronic venous insufficiency. *Angiology* 2001; 52 (Suppl. 1): s49–56 [LIT R].
6. Wright DD, Franks PJ, Blair SD et al. Oxerutins in the prevention of recurrence in chronic venous ulceration: randomized clinical trial. *Br J Surg* 1991; 78: 1269–70 [RCT].

Guideline #7c.4: Fibrinolytic enhancement with an anabolic steroid such as stanozolol in conjunction with compression therapy may be useful in treating lipodermatosclerosis associated with venous ulcers. However, one must be aware of side effects (Level II).

Principle: A fibrinolytic agent capable of decreasing extravascular fibrin should be able to decrease induration and inflammation in cases of lipodermatosclerosis.

Evidence:

1. Burnand K, Clemenson G, Morland M et al. Venous lipodermatosclerosis: treatment by fibrinolytic enhancement and elastic compression. *Br Med J* 1980; 280: 7–11 [RCT].
2. Layer GT, Stacey MC. Stanozolol and treatment of venous ulceration: interim report. *Phlebology* 1986; 1: 197–203 [RCT].
3. Kirsner RS, Pardes JB, Eaglstein WH et al. The clinical spectrum of lipodermatosclerosis. *J Am Acad Dermatol* 1993; 28: 623–7 [LIT REV].
4. Hefman T, Falanga V. Stanolozol as a novel therapeutic agent in dermatology. *J Am Acad Dermatol* 1995; 33: 254–8 [LIT REV].
5. Segal S, Cooper J, Bolognia J. Treatment of lipodermatosclerosis with oxandrolone in a patient with stanolozol-induced hepatotoxicity. *J Am Acad Dermatol* 2000; 13: 588–9 [RETRO S].

Guideline #7c.5: Oral zinc supplementation is not useful in the treatment of venous leg ulcers (Level I).

Principle: Adding zinc to patients without a deficient total body zinc reservoir will not improve healing of chronic wounds such as venous ulcers.

Evidence:

1. Wilkinson EA, Hawke CI. Oral zinc for arterial and venous leg ulcers. *The Cochrane Database of Systematic Reviews Issue 2*. The Cochrane Collaboration: John Wiley & Sons Ltd., 2000 [STAT].
2. Phillips A, Davidson M, Greaves MW. Venous leg ulceration: Evaluation of zinc treatment, serum zinc and rate of healing. *Clin Exp Dermatol* 1977; 2: 395–9 [RCT].
3. Myers MB, Cherry G. Zinc and healing of chronic leg ulcers. *Am J Surg* 1970; 120: 77–81 [RCT].
4. Greaves MW, Ive PA. Double-blind trial of zinc sulphate in the treatment of chronic venous ulceration. *Br J Dermatol* 1972; 87: 632–4 [RCT].

GUIDELINES FOR LONG-TERM MAINTENANCE IN TREATMENT OF VENOUS ULCERS

Preamble: Venous ulcers of the lower extremity are a chronic, long-term problem. Recurrence rates are as high as 70%. Therefore, long-term maintenance must be addressed even for healed ulcers.

Guideline #8.1: Patients with healed or surgically repaired venous ulcers should use compression stockings constantly and forever (Level I).

Principle: Most treatments do not eliminate the underlying increased ambulatory venous pressure (venous hypertension), so a degree of compression is necessary long term.

Evidence:

1. Nelson EA, Bell-Syer SE, Cullum NA. *The Cochrane Database of Systematic Reviews, Issue 4*. The Cochrane Collaboration: John Wiley & Sons Ltd., 2000 [STAT].
2. Samson RH, Showalter DP. Stockings and the prevention of recurrent venous ulcers. *Dermatol Surg* 1996; 22: 373–6 [RCT].
3. Franks PJ, Oldroyd MI, Dickson D et al. Risk factors for leg ulcer recurrence: a randomized trial of two types of compression stocking. *Age Aging* 1995; 24: 490–4 [RCT].
4. Mayberry JC, Moneta GL, Taylor LM et al. Fifteen-year results of ambulatory compression therapy for chronic venous ulcers. *Surgery* 1991; 109: 575–81 [CLIN S].
5. Kurz X, Kahn SR, Abenhaim L et al. Chronic venous disorders of the leg: epidemiology, outcomes, diagnosis, and management. Summary of an evidence-based report of the VEINES task force venous insufficiency, epidemiologic, and economic studies. *Int Angiology* 1999; 18: 83–102 [STAT].

Guideline #8.2: Exercises to increase calf muscle pump function have been demonstrated to be helpful in long-term maintenance and venous ulcer prevention (Level III).

Principle: Calf muscle pump function has been shown to be improved with exercises.

Evidence:

1. Padberg FT, Johnston MV, Sisto SA. Structured exercise improves calf muscle pump function in chronic venous insufficiency: a randomized trial. *J Vasc Surg* 2004; 39: 79–87 [RCT].
2. Yang D, Vandongen YK, Stacey MC. Effect of exercise on calf muscle pump function in patients with chronic venous disease. *Br J Surg* 1999; 86: 338–44 [CLIN S].

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