SUMMARY

Background: Chronic leg ulcers are defined as those that show no tendency to heal after 3 months of appropriate treatment or are still not fully healed at 12 months. In this article, we present an approach to the challenging problem of chronic leg ulcers that is based on the principles of evidence-based medicine, i.e., the explicit use of the best available scientific evidence as a guide to treatment.

Methods: Selective review of the relevant literature, including current guidelines and meta-analyses, concerning diagnostic and therapeutic strategies for chronic leg ulcers.

Results: The main types of causally directed treatment are: vein surgery to eliminate pathological reflux, interventions to improve the circulation in arterial occlusive disease, and treatment of underlying diseases, such as diabetes mellitus.

Conclusion: Physicians providing modern evidence-based management of chronic leg ulcers should make use of their own clinical experience in combination with the best current scientific evidence. It seems clear that the many available treatment options should be evaluated critically in an interdisciplinary setting. In particular, causally directed treatment must be provided in addition to symptomatic, stage-based local wound treatment.

► Cite this as:
TABLE 1

<table>
<thead>
<tr>
<th>Causal treatment options of chronic venous leg ulcers</th>
<th>Modalities of the causal treatment</th>
<th>level of evidence / grade of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compression therapy</td>
<td>Phlebological compression bandages, medical compression stockings, intermittent pneumatic compression</td>
<td>Ia/A</td>
</tr>
<tr>
<td>Varicose surgery</td>
<td>Crossection and surgical stripping of the saphenous veins, selective varicose exresis, mini-phlebectomy, CHIVA, perforator vein division, sub-fascial endoscopic perforator surgery (SEPS)</td>
<td>Ib/A</td>
</tr>
<tr>
<td>Endovascular therapies</td>
<td>Endovascular laser therapy (various laser systems), radiofrequency ablation, radiofrequency-induced thermotherapy (RFITT)</td>
<td>Ib/A</td>
</tr>
<tr>
<td>Sclerosing therapy</td>
<td>Injection sclerotherapy, ultrasound-guided foam sclerotherapy (direct puncture, catheter sclerosing)</td>
<td>Ib/A</td>
</tr>
<tr>
<td>Surgical ulcer treatment</td>
<td>Shaving surgery with graft coverage, ulcer excision with fasciectomy with graft coverage</td>
<td>III/B</td>
</tr>
</tbody>
</table>

* Based on the evidence classification of the Oxford Centre for Evidence-Based Medicine

Evidence level:
- Ia: Evidence from meta-analyses of several randomized controlled trials
- Ib: Evidence based on at least one randomized controlled trial
- Iib: Evidence based on at least one well-designed but not randomized and controlled trial
- IIb: Evidence based on at least one well-designed quasi-experimental trial
- III: Evidence based on well-designed, non-experimental descriptive trials such as comparative studies, correlation studies or case-control studies
- IV: Evidence based on reports in expert panels or expert opinions or clinical experience of recognized authorities

**Recommendation grade:**
- A: Key recommendation: there is at least one randomized controlled trial of overall good quality (evidence levels Ia and Ib)
- B: Preferred recommendation: there are well-implemented clinical trials with direct reference to the recommendation (evidence levels II or III)
- C: Optional recommendation: expert opinion and/or clinical experience of recognized authorities (evidence level IV) or extrapolation from evidence levels Ia, Iib or III; this classification indicates that directly applicable clinical trials of good quality do not exist or are not available.

A wound that is present for more than three months is considered chronic (7). The clinically most significant chronic wounds in terms of epidemiology and health economics are venous stasis ulcers, wounds and wound healing disorders in diabetes mellitus, and pressure ulcers in immobile patients with reduced general condition (5).

In general, evidence-based management of chronic wounds includes the following:
- Comprehensive diagnosis, medical history and documentation of findings [III; B]
- Relevant data include pain, allergization and tetranus vaccine protection [I; A]
- Known thrombophilia [I; A]

Decreased levels of zinc, iron, folate, albumin, vitamin C and selenium as a result of poor diet must be eliminated in cases of large (>100 cm²) ulcers and corrected if necessary (3).

The significance of bacterial colonization of chronic wounds is unclear as is the use of antiseptics [IV; C]. Debridement, also using maggots (biosurgery) or vacuum-assisted closure (VAC) technique, is recommended in cases of wound infection [Ib; A]. Wound debridement is, however, recommended in general [III, B] as is maintaining a moist wound environment [Ia, A].

**Refractory and/or morphologically abnormal ulcerations must be histologically evaluated [I, A].**

**Venous stasis ulcers**

Venous ulcers are the result of ambulatory venous hypertension with chronic venous insufficiency (CVI). Venous ulcerations generally develop on skin that typically exhibits the stigmata of CVI such as hyperpigmentation, varicose eczema, lipodermatosclerosis or atrophic blanche. The skin around the ulcer therefore exhibits typical trophic changes. Problems are caused by refractory ulcers that do not show signs of healing after 3 months’ therapy or have not healed after 12 months of adequate treatment. The information about evidence in the following section refers to the S3 guideline for the diagnosis and treatment of venous stasis ulcers (3).

**Diagnosis**

As a matter of principle extensive vascular Doppler or duplex ultrasonographic imaging is required. In addition, phlebological diagnosis is used not only to precisely determine the clinical symptoms but also to plan causal treatment procedures [II; B].

**Causal treatment**

Reducing the pressure and volume overload in the venous system is the main causal treatment (8) [Ia; A]. This can be achieved using compression therapy (phlebological compression bandages, medical compression of current clinical medicine based on clinical trials and medical publications that confirm or refute facts.

Because the whole body of medical knowledge is currently doubling in size every five years, however (6), even a skillful physician feels increasingly overwhelmed when trying to determine what is significant amongst the abundance of existing and emerging knowledge.

Information about the evidence supporting diagnostic approaches and the safety and efficacy of treatments is most important for the management of chronic wounds.

Hierarchical levels of evidence and different grades of recommendations are differentiated for different treatment modalities. Level of evidence and recommendation grades are indicated in the following in square brackets. An overview of evidence levels and recommendation grades is provided in Table 1.
stockings) or using targeted correction of pathological reflux (Table 1).

**Conservative causal treatment**

Compression therapy is still considered the basic treatment for venous ulcers, and its ability to heal venous ulcers is clearly supported by a body of evidence from many studies (9). The healing rate increases and the recurrence rate decreases with increasing interface pressures of the compression bandages or stockings [Ia; A]. A meta-analysis showed that adequate compression therapy is not only important for the healing of venous stasis ulcers but that continuing the compression after the ulcer has healed is also critical for the recurrence-free interval.

Compression stockings have proven to be effective for venous ulcers (10). The benefits of compression stocking therapy with venous stasis ulcers are derived both from the constant pressure of the stocking and better compliance of patients (e6) [Ia; A].

**Surgical causal treatment**

The aim is to eliminate venous reflux because reflux is relevant to prevent wound healing and causes a considerable increase in the ulcer recurrence rate. The effects of varicose correction measures on venous hemodynamics can be determined using duplex ultrasonography, or plethysmographically, or using direct venous pressure measurement.

The efficacy of all types of reflux correction measures in terms of accelerated ulcer healing has been proven (11). The choice of method can therefore be tailored according to benefits and drawbacks in each individual patient. Classical surgical techniques, endovascular thermal procedures (e7, 12), and (foam) sclerotherapy (13) are all options [Ib; A]. There is less benefit gained from regenerating the superficial venous system in patients with an insufficient deep venous system than in patients with a sufficient deep venous system in terms of the healing of venous stasis ulcers and in terms of the prolongation of the recurrence-free interval [IIa; B].

The significance of insufficient perforating veins in hemodynamics and the relevance of isolated treatment of these veins has not been clarified [Ia; A].

**Surgical ulcer treatment**

If a trophic disorder (dermatolipofasciolsclerosis) is present around the ulcer, radical ablation of the entire trophically destroyed tissue with subsequent coverage of the defect is recommended [II; B]. The use of tangential excision of the affected tissue has become established as shave therapy (Figures 1 and 2). This technique accelerates ulcer healing. Simultaneous removal of the crural fascia is optional and is still controversial (14, 15) [III; B].

Coverage of the defect using autologous mesh grafts is preferable to a full-thickness skin transplant and transplantation of free vascularized musculofasciocutaneous flaps because it achieves comparable results with less effort [III; B].

**Symptomatic treatment**

The requirements for ideal wound dressings are listed in Box 1.

Suitable dressing materials include non-medicated paraffin gauze, foams, alginates, hydrogels, hydrocolloids, and hydroactive dressings. Wound dressings that provide a moist wound environment have been proven to have a general benefit. There is also consensus about the need for an appropriate balance in the moisture content of the dressing. There is evidence of pain reduction with the use of hydrocolloidal and foam wound dressings [Ia; A]. General superiority of one particular wound dressing compared to another has not yet been demonstrated (16) [Ia; A]. However, physicians must be mindful of the high sensitization rate to external dressings and their constituents in ulcer patients [I; A]. There is thus an increased risk of developing type IV allergies in the form of allergic contact eczema around the ulcer.

**Chronic wounds in diabetes mellitus**

Poorly healing ulceration, predominantly around the feet, can develop as a complication of diabetes. Often
amputation is the last resort (2, e3). The risk of reamputation in patients with diabetes is high. In a longitudinal study the cumulative risk of being reamputated was 27% after one year, 48% after 3 years, and 61% after 5 years (17). The risk factors for diabetic foot ulcer are listed in Table 2. Peripheral sensorimotor neuropathy is particularly important [III; B]. Polyneuropathy without concomitant vascular disease often gives rise to the development of diabetic foot ulcer. Repeated trauma, which is often not perceived, leads to the formation of excessive callusing (Figure 3). Subkeratotic hematomas develop below these calluses as a result of the persistent action of pressure and shear forces. Finally, ulceration develops at the exposed sites (e8). The most important cause of foot ulceration is unsuitable footwear [II; A]. Information about evidence for the following section is based on the German treatment guideline for type 2 diabetes and the guideline for diabetic foot syndrome from the German Diabetes Association (2, e3, 4).

Diagnostic clarification
As for venous ulcers, a vascular examination of the vessels supplying blood to the extremities is also required with diabetic foot. As a matter of priority, Doppler-derived arterial wedge pressures with calculation of the ankle/brachial index should be measured [II; B] while taking into account any potential medial sclerosis.

The diagnostic criteria for diabetic neuropathy that are of particular relevance for diabetic foot syndrome include, analogous to the Neuropathy Deficit Score

**Recognition**
- A history of diabetes is important.
- A history of necrotic foot ulcerations is important.
- A history of previous amputations is important.

**Observation**
- Inspect the lower extremities for any signs of foot ulceration.
- Inspect the lower extremities for any signs of callus formation.

**Palpation**
- Palpate the lower extremities for any signs of increased pressure.
- Palpate the lower extremities for any signs of decreased sensation.

**Sensation**
- Test the lower extremities for any signs of decreased sensation.
- Test the lower extremities for any signs of decreased pain perception.

**Temperature**
- Test the lower extremities for any signs of decreased temperature.
- Test the lower extremities for any signs of increased temperature.

**Vibration**
- Test the lower extremities for any signs of decreased vibration perception.
- Test the lower extremities for any signs of increased vibration perception.

**Sensation**
- Test the lower extremities for any signs of decreased vibration perception.
- Test the lower extremities for any signs of increased vibration perception.

**Reflexes**
- Test the lower extremities for any signs of decreased reflexes.
- Test the lower extremities for any signs of increased reflexes.

**Nerve Conduction Velocity**
- Test the lower extremities for any signs of decreased nerve conduction velocity.
- Test the lower extremities for any signs of increased nerve conduction velocity.

**Skin Temperature**
- Test the lower extremities for any signs of decreased skin temperature.
- Test the lower extremities for any signs of increased skin temperature.

**Blood Flow**
- Test the lower extremities for any signs of decreased blood flow.
- Test the lower extremities for any signs of increased blood flow.

**Neuropathy Deficit Score**
- Score the lower extremities for any signs of decreased sensation.
- Score the lower extremities for any signs of decreased pain perception.
- Score the lower extremities for any signs of decreased vibration perception.
- Score the lower extremities for any signs of decreased reflexes.
- Score the lower extremities for any signs of decreased nerve conduction velocity.
- Score the lower extremities for any signs of decreased skin temperature.
- Score the lower extremities for any signs of increased blood flow.

**Diabetic Foot Syndrome**
- A history of diabetes is important.
- A history of necrotic foot ulcerations is important.
- A history of previous amputations is important.

**Observation**
- Inspect the lower extremities for any signs of foot ulceration.
- Inspect the lower extremities for any signs of callus formation.

**Palpation**
- Palpate the lower extremities for any signs of increased pressure.
- Palpate the lower extremities for any signs of decreased sensation.

**Sensation**
- Test the lower extremities for any signs of decreased sensation.
- Test the lower extremities for any signs of decreased pain perception.

**Temperature**
- Test the lower extremities for any signs of decreased temperature.
- Test the lower extremities for any signs of increased temperature.

**Vibration**
- Test the lower extremities for any signs of decreased vibration perception.
- Test the lower extremities for any signs of increased vibration perception.

**Reflexes**
- Test the lower extremities for any signs of decreased reflexes.
- Test the lower extremities for any signs of increased reflexes.

**Nerve Conduction Velocity**
- Test the lower extremities for any signs of decreased nerve conduction velocity.
- Test the lower extremities for any signs of increased nerve conduction velocity.

**Skin Temperature**
- Test the lower extremities for any signs of decreased skin temperature.
- Test the lower extremities for any signs of increased skin temperature.

**Blood Flow**
- Test the lower extremities for any signs of decreased blood flow.
- Test the lower extremities for any signs of increased blood flow.

**Neuropathy Deficit Score**
- Score the lower extremities for any signs of decreased sensation.
- Score the lower extremities for any signs of decreased pain perception.
- Score the lower extremities for any signs of decreased vibration perception.
- Score the lower extremities for any signs of decreased reflexes.
- Score the lower extremities for any signs of decreased nerve conduction velocity.
- Score the lower extremities for any signs of decreased skin temperature.
- Score the lower extremities for any signs of increased blood flow.

**Summary**
- Diabetic foot syndrome is a complex condition that requires a comprehensive approach.
- Early detection and intervention are crucial.
- Prevention strategies should be implemented.

**References**

**Table 2**
<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk assessment and clinical parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor glycemic control</td>
<td>HbA1c</td>
</tr>
<tr>
<td>Previous ulcer/amputation</td>
<td>Medical history, physical examination</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Abnormal sensorimotor perception of vibration</td>
</tr>
<tr>
<td>Reduction in visual acuity</td>
<td>Ophthalmological examination</td>
</tr>
<tr>
<td>Trauma</td>
<td>Poorly fitting shoes, pressure, burns</td>
</tr>
<tr>
<td>Biomechanics</td>
<td>Limited joint mobility, bony prominences, foot deformity/osteoarthritis, callus</td>
</tr>
<tr>
<td>Peripheral arterial occlusive disease</td>
<td>Ankle-brachial index</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td>Poor access to medical facilities, lack of compliance/neglect, no or inadequate education</td>
</tr>
</tbody>
</table>

**Table 3**
| Classification of diabetic ulcers according to Wagner and Armstrong (e10) |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
|                            | 0                           | 1                           | 2                           | 3                           | 4                           | 5                           |
| A                           | Callus or scar              | Superficial wound           | Wound penetrating to tendon/capsule | Wound penetrating to bone/joint | Necrotic foot areas         | Necrotic foot, entire       |
| B                           | Infection                   | Infection                   | Infection                   | Infection                   | Infection                   | Infection                   |
| C                           | Ischemia                    | Ischemia                    | Ischemia                    | Ischemia                    | Ischemia                    | Ischemia                    |
| D                           | Infection + ischemia        | Infection + ischemia        | Infection + ischemia        | Infection + ischemia        | Infection + ischemia        | Infection + ischemia        |

**Figure 3:** Hyperkeratosis with bleeding and incipient ulceration with diabetic neuropathy.
(NDS), examination of the achilles tendon reflex, and vibration, pain, temperature and touch perception. Examination of the achilles tendon reflex using a reflex hammer is used to determine the depth sensitivity. Vibration perception is examined using biothesiometry which has a high predictive value for ulcer formation (e9) [III; A]. The Rydel-Seiffer tuning fork is a simple and practical alternative to biothesiometry [Ib; A]. It also makes sense to differentiate the neuropathic and arterial risk factors. In addition, the wound should be classified using the Wagner and Armstrong classification system. The conventional classification by Wagner describes diabetic foot ulcers based on the extent of existing tissue destruction. The University of Texas Wound Classification System (the Armstrong classification) is superior to the Wagner classification in terms of an estimate of the likely success of treatment because of the additional description of infection and ischemia (Table 3) (18).

Vascular causal treatment
Appropriate systemic therapy [Ia; A], interventional or surgical revascularization [III; A] should be implemented with verified hemodynamically relevant peripheral arterial occlusive disease (PAOD).

Biomechanical treatment options/pressure relief
Several studies have confirmed the importance of pressure relief for the healing of diabetic ulcers [III; B]. Patient education is also critical [II; A]. The patient must understand that even a few weight-bearing steps on an ulcerated foot can delay healing. The effectiveness of the biomechanical approach is therefore highly dependent on patient compliance.

An important study about pressure relief demonstrated using hidden activity sensors in a double-shelled total-contact cast (TCC) that the TCC was actually only worn on average for 28% of daily activities (e10). Very good data are available for the non-removable cast or walker. They revealed outstanding healing rates using two non-removable relieving aids with no difference between a TCC and TCC with an additional fixed ready-made mobility orthosis (19) [III; A].

Symptomatic treatment
The same guidelines apply to the local treatment of diabetic foot ulcer as in chronic venous ulcer. Amputation should be considered as a symptomatic treatment option if no improvement could be achieved despite consistent causal treatment or if there is a risk of a severe systemic infection arising from the wound [III; B].

Secondary prophylaxis
Secondary prophylaxis plays a critical role for patients with diabetes in light of the high recurrence rates and the high risk of developing an additional foot ulcer. Regular check-ups are recommended in accordance with the particular risk profile (Table 4). It is important to ensure the patient is aware of his/her disease and the importance of adequate pressure relief.

### TABLE 4

<table>
<thead>
<tr>
<th>Risk profile</th>
<th>Examinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non sensory neuropathy</td>
<td>1×/year</td>
</tr>
<tr>
<td>Sensory neuropathy</td>
<td>Every 6 months</td>
</tr>
<tr>
<td>Sensory neuropathy and signs of peripheral arterial occlusive disease and/or foot deformities</td>
<td>Every 3 months</td>
</tr>
<tr>
<td>Previous ulcer</td>
<td>Every 1 to 3 months</td>
</tr>
</tbody>
</table>

### BOX 2

Clinical stages of pressure ulcers*

- **Stage 1**
  - Non-blanchable erythema of intact skin. Skin discolorations, warmth, edema or induration can also be indicators of stage 1, particularly in dark-skinned individuals.

- **Stage 2**
  - Partial-thickness loss of skin with damage to the epidermis and/or the dermis. The ulcer is superficial and presents clinically as an abrasion or blister.

- **Stage 3**
  - Full-thickness loss of skin including damage to or necrosis of the subcutaneous tissue that may extend to, but not through, the fascia.

- **Stage 4**
  - Extensive tissue necrosis possibly including muscle, bone or supporting structures

*Classification from the Pressure Ulcer Treatment Guidelines (EPUAP 1998)

Pressure ulcers of the leg

A pressure ulcer is a site of localized damage to the skin and/or the underlying tissue, usually over a bony prominence as a result of pressure, shearing forces, and/or friction. Pressure ulcers are divided into four stages based on the definitions of the European Pressure Ulcer Advisory Panel (Box 2).

A range of influential factors are associated with a pressure ulcer, the significance of which have not yet been definitively clarified (20). Although risk assessments are recommended, randomized controlled trials that would verify their benefit have not been published to date (20). The most important endogenous risk factor for the development of a leg ulcer is peripheral sensorimotor neuropathy such as that which occurs in diabetes mellitus, for example. The only facts verified with a high level of evidence are that pressure relief by repositioning protects against a pressure ulcer and that mattresses with higher specifications have a greater protective effect than standard foam mattresses (21) [III; B].
Even if the problems and their prevention and treatment are known and recognized in principle, there is nevertheless no solid evidence verified by appropriate studies for diagnostic and therapeutic approaches (21, 22). The following comments are based primarily on expert opinions, case-control studies, or randomized controlled trials with low power. The use of electrical stimulation, which has demonstrably enhanced wound healing in pressure ulcers, is an exception (e11).

Prevention of pressure damage to the skin and the underlying tissue is an essential part of treatment in at-risk patients. Adequate risk assessment and subsequent risk reduction is crucial (23).

Conservative causal treatment
The foundation of any pressure ulcer treatment is targeted local pressure relief by repositioning and the use of aids (24). In contrast, wound cleansing does not appear to play a critical role (e12).

Surgical causal treatment
Surgical strategies should be considered for pressure ulcers from stage II onwards that do not heal using conservative measures. If no tendency to heal becomes apparent using surgical debridement with the aid of the above named conservative measures, plastic surgery reconstruction is indicated where appropriate. Surgical measures must be planned and undertaken in the context of the general condition of the patient. Geriatric patients in particular often suffer from multiple comorbidities.

Symptomatic treatment / local treatment
For local treatment absolute pressure relief is critical for wound healing, otherwise the same guidelines apply as for chronic venous ulcers (24).

Summary
The treatment of chronic wounds of the lower extremities still presents a therapeutic challenge. There is clear evidence suggesting that causal treatment should have priority. A comprehensive diagnostic evaluation including vascular, metabolic and physical aspects is therefore essential at the start of treatment.

With ulcers that are predominantly venous in origin, reduction of venous hypertension is critical, with compression therapy occupying an important place in achieving this. Modern compression stocking systems supplied by various manufacturers are promising. Nevertheless, options such as plastic surgery and shave therapy for venous ulcers, which has “only” evidence level III, is an important component of the overall treatment plan.

Appropriate pressure relief has priority for neuropathic, diabetic or pressure ulcers.

Conflict of interest statement
PD Kahle receives sponsorship for conferences from the following companies: Bauerfeind AG Phlebologie, BSN-JOBST GmbH, Chemische Fabrik Kreussler GmbH, Karl Reisse GmbH & Co KG, Söring GmbH Medizintechnik, Paul Hartmann AG, URGOS GmbH, OMS Pharma, medi GmbH & Co. KG, Villa sana GmbH & Co. medizinische Produkte KG, Chemische Fabrik Kreussler GmbH, Bühringer Ingelheim Pharma GmbH & Co. KG.

She also received honoraria for speaking from: Bauerfeind AG Phlebologie, Johnson and Johnson, Ethicon, BSN-JOBST GmbH, Medi GmbH & Co. KG, and Chemische Fabrik Kreussler GmbH.

Dr. Hermanns and Dr. Gallenkemper declare that no conflict of interest exists.

Manuscript received on 26 April 2010, revised version accepted on 30 November 2010.

Translated from the original German by language & letters.

REFERENCES

KEY MESSAGES

- For refractory and/or morphologically abnormal ulcerations malignancies must be histologically excluded.
- Information about the evidence supporting diagnostics, the safety, and the efficacy of treatments is most important for the management of chronic wounds.
- A precise diagnosis is essential for the planning of individualized causal treatment.
- For venous stasis ulcers treatment of venous hypertension using compression together with reflux correction has priority.
- For foot ulcerations in diabetes mellitus pressure relief around the wound is important for healing.

Corresponding author
PD Dr. med. Birgit Kahle
Universitätsklinikum Schleswig-Holstein
Campus Lübeck
Klinik für Dermatologie, Allergologie und Venerologie
Ratzeburger Allee 160 (Haus 10)
23538 Lübeck, Germany

For eReferences please refer to: www.aerzteblatt-international.de/ref1411
Evidence-Based Management of Chronic Leg Ulcers

Birgit Kahle, Hans-Joachim Hermanns, Georg Gallen kemper

eReferences

e1. www.weyergans.ch/upload/publikationen/BonnerVenenstudie.pdf


