The American Journal of Surgery 188 (Suppl to July 2004) 9S-17S

# Protocol for the successful treatment of pressure ulcers

Harold Brem, M.D.a.\*, Courtney Lyder, R.N., N.D.b

<sup>a</sup>Department of Surgery, Columbia University College of Physicians & Surgeons, 5141 Broadway, New York, New York 10034, USA

<sup>b</sup>Acute and Specialty Care of Adults Division, University of Virginia School of Nursing, Charlottesville, Virginia, USA

#### **Abstract**

Bed-bound patients with pressure ulcers are almost twice as likely to die as are those without pressure ulcers. If pressure ulcers are treated with a comprehensive regimen upon early recognition, nearly all stage IV ulcers can be avoided. Furthermore, such a regimen can significantly reduce the comorbidities, mortalities, and costs of treatments resulting from stage IV ulcers. The costs of treatments for comorbidities after the ulcer progresses to stage IV far outweigh the costs for early treatment of the ulcer before it progresses beyond the early stages. We describe herein the 4 stages of pressure ulcers, as well as the pathogeneses, costs, and complications associated with these wounds. A comprehensive 12-step detailed protocol for treatment of pressure ulcers is described; this includes recognizing that every patient with limited mobility is at risk for developing a sacral, ischial, trochanteric, or heel ulcer; daily assessment of the skin; objective measurement of every wound; immediate initiation of a treatment protocol; mechanical debridement of all nonviable tissue; establishment of a moist wound-healing environment; nutritional supplementation for malnourished patients; pressure relief for the wound; elimination of drainage and cellulitus; biological therapy for patients whose wounds fail to respond to more traditional therapies; physical therapy; and palliative care. Availability of the described treatment modalities, in combination with early recognition and regular monitoring, ensures rapid healing and minimizes morbidity, mortality, and costs. © 2004 Excerpta Medica, Inc. All rights reserved.

Pressure ulcers are often undertreated. A pressure ulcer is a break in the integument usually caused by continuous pressure to skin and muscle. Although these ulcers can occur anywhere on the body, they are often located in the trochanteric, ischial, heel, and sacral areas. Patients may not immediately be aware of these developing wounds, because they often occur in bed-bound, paralyzed, and elderly patients undergoing treatment for other diseases.

The prevalence of pressure ulcers in the United States is estimated to be 1.3 million to 3 million [1]. The incidence of pressure ulcers is estimated to be 5% to 10% among hospitalized patients [2–7], 13% among those in nursing homes [8], and up to 39% among those with spinal-cord injuries [9,10]. Pressure ulcers can cause pain and loss in economic productivity, and also can result in huge expenditures for patients as well as hospitals [11].

Pressure ulcers are the source of numerous complications, which result in long-term, frequent, and/or multiple hospital admissions. A new pressure ulcer is estimated to increase a patient's hospital stay by nearly a factor of 5 [12].

E-mail address: hb2133@columbia.edu

This work was supported by the United Spinal Association.

Patients with pressure ulcers generally have significantly poorer physical function, are less able to perform self-care, and are less mobile [13]. More than half (51%) of the long-term care–facility patients with pressure ulcers have methicillin-resistant *Staphylococcus aureus* (MRSA) infection [14]. Furthermore, pressure ulcers are correlated with >2-fold rates of increased mortality [15,16], independent of the source of the ulcer.

The reasons patients with pressure ulcers have increased length of stay are multifold. The most common reason is that when a patient with a pressure ulcer has a low-grade fever and/or increased white blood cell count with left shift, they are misdiagnosed with pneumonia or urinary tract infection. Most commonly, they need an operative debridement to remove all nonviable tissue with its associated massive bacterial contamination. It is then that topical therapy and local wound care is most effective. The most dangerous aspect of treatment with antibiotics for a misdiagnosed pneumonia or urinary tract infection, and not with appropriate surgical debridement, is the promotion of resistant bacteria within the ulcer.

All bed-bound patients are at risk for developing pressure ulcers. The most important component of pressure ulcer care is daily examination of the trochanteric, ischial, sacral, and heel areas. If the slightest break in the integu-

<sup>\*</sup> Corresponding author. Tel.: +1-212-932-5094; fax: +1-212-658-9806.

ment is detected, treatment must be initiated immediately, followed by daily documentation of subsequent changes (eg, measurement of contraction and epithelialization) to ensure appropriate treatment and prevent the ulcer from progressing.

Healthcare providers are often reluctant to diagnose pressure ulcers for fear of being blamed for their development and because legal professionals are increasingly demanding accountability for healthcare interventions [17]. Although healthcare practitioners must be accountable for their actions, contributing factors such as age, immobility, and frailty also must be taken into account when incidence is calculated and analyzed.

As the elderly population continues to grow at an unprecedented rate, there will inevitably be more chronically and critically ill patients in the healthcare system. Because these populations are at higher risk of developing pressure ulcers, the establishment of a comprehensive protocol for treatment of pressure ulcers is imperative. Whereas prevention remains the ideal goal [1], our protocol emphasizes early detection and treatment, which may halt ulcer progression and its ensuing morbidities, mortalities, and costs (Fig. 1).

## Pressure ulcer stages

Pressure ulcers are generally classified according to the degree of tissue damage involved. Accurate initial assessment of a patient's wound is crucial in comprehensive treatment. The following is based on the National Pressure Ulcer Advisory Panel staging definitions:

- Stage I: Nonblanchable erythema of intact skin, intact epidermis. Coloration is pink, red, or mottled after pressure is relieved. For patients with darker pigmentation, discoloration of the skin, warmth, edema, induration, or hardness may also be indicators.
- Stage II: Partial-thickness skin loss involving epidermis, dermis, or both. The skin is broken, cracked, blistered, and mottled in color. Necrotic tissue or drainage also may be present. The ulcer remains superficial and presents as an abrasion, blister, or shallow crater.
- Stage III: Full-thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia. The ulcer presents clinically as a deep crater with or without undermining of adjacent tissue.
- Stage IV: Full-thickness skin loss with extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures (eg, tendon, joint capsule).
   Undermining and sinus tracts may also be associated with stage IV ulcers [17].

Table 1 Costs related to treatment and management of pressure ulcers

- · Wound dressings
- Management of bacterial colonization and systemic infection (eg, blood cultures)
- Care by health professionals
- Diagnostic procedures (eg, x-rays)
- · Therapeutic procedures
- Medications (analgesics, antibiotics)
- Treatment of secondary infections (eg, renal failure, pneumonia)
- Lawyer fees
- Delayed treatment

#### Costs

Pressure ulcers are the second most common cause for hospital readmissions, with treatment costs that range from \$20,000 to \$70,000 per wound [18]. In addition, costs of treating the associated complications in a single hospital stay from a pressure ulcer often exceed \$200,000 per patient (this occurs in select cases in which the ulcer is not recognized initially and complications from the wound develop) [19]. These costs related to pressure ulcers place a tremendous financial burden on the healthcare system. An assessment of cost-of-illness of pressure ulcers in the Netherlands ranged from a low of \$362 million to a high of \$2.8 billion, which accounted for approximately 1% of the total Dutch healthcare budget [20]. A study of 30 patients with 45 pressure ulcers reported the mean cost of treatment, including long-term care and hospital costs, at \$2,731 per ulcer. When hospital costs were excluded, the mean cost of treatment was calculated at \$489 per ulcer [21]. These figures clearly indicate that pressure ulcers present a serious financial problem.

When assessing the total cost of pressure ulcers, it is important to consider the costs of nontreatment. Although a small ulcer (eg, stage I or II) in a critically ill patient is generally not considered a significant clinical problem, if this ulcer progresses to the bone, which often occurs without early intervention and a well-documented and effective treatment plan, the ulcer can result in significant costs, morbidity, and mortality. For example, the cost of treating stage IV ulcers has been reported to be 10 times that of treating stage II ulcers [21]. Moreover, wounds that progress to stage IV are more difficult to treat effectively than those treated successfully at earlier stages. Therefore, early recognition and treatment are mandatory to minimize costs, as well as prevent progression and accelerate healing of these pressure ulcers (Table 1).

#### **Pathogenesis**

A pressure ulcer is, by definition, a chronic wound and therefore has underlying physiologic impairments that affect the wound-healing process. Intervention is always nec-

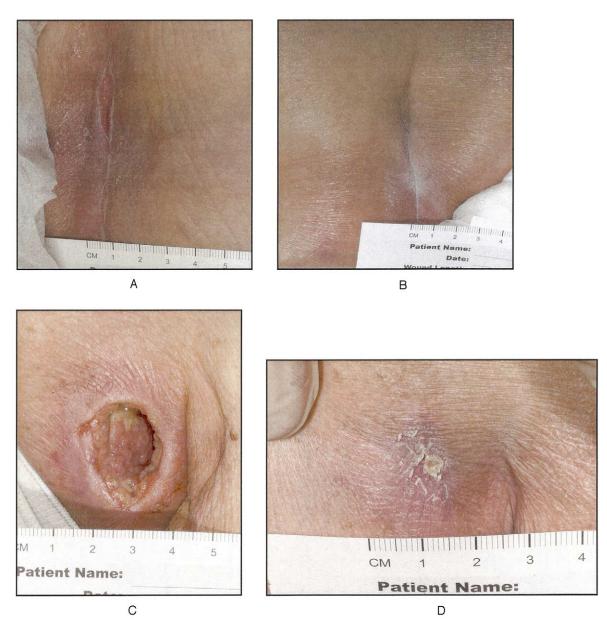


Fig. 1. Pressure ulcers present with many etiologies. In the protocol outlined, the treatment is almost always the same regardless of etiology. Specifically, it is the basis of this protocol that all new pressure ulcers be treated immediately upon recognition. (A) A 91-year-old woman with sacral ulcer. This patient was treated immediately, and subsequently her venous stasis ulcer healed rapidly (B) under the protocol. No debridement or culture was needed. This is a typical example of how early treatment halts ulcer progression. This patient became progressively wheelchair-bound and was instructed to report any new break in the skin. Almost all pressure ulcers present in a similar fashion, ie, as a break in the skin. (C) In contrast to the case depicted in A and B, this previously healthy 96-year-old man had also become progressively wheelchair-bound but presented with an infected stage IV pressure ulcer requiring operative debridement. He healed on the protocol (D) but would have avoided the morbidity and expense of a stage IV ulcer if he had presented upon first recognition. This case also emphasizes that every wheelchair- or bed-bound patient must be examined daily and the protocol initiated immediately upon recognition of a break in the skin.

essary to prevent progression. Pressure alone does not account for distribution of nonhealing wounds in the lower back. For instance, the sacrum, which has less pressure than the scapula, is a site in which pressure ulcers occur much more frequently. It has been established experimentally that the angiogenic response is dependent on anatomical location and is attenuated significantly in the lower, as compared with upper, dorsum [22,23]. Also reported is that

wound healing is slowed in the lumbosacral area, which may in part be the result of decreased angiogenic response in the area [24].

Elderly patients are generally considered to have an impaired ability to heal their wounds. This impairment can further be exacerbated by their decreased capability of handling the complications, such as cellulitis and sepsis, associated with these pressure ulcers. For this reason, it is

crucial that therapy for the elderly be initiated immediately [25].

Chronic wounds in patients with serious illnesses are often allowed to progress because the main focus of hospitalization is on the admitting illness. Both the healthcare staff and the patient must be trained to detect these ulcers early in order to prevent progression to more serious stages. Daily observation should continue at home. Patients must be trained to evaluate themselves with palpation and mirrors to detect newly developing pressure ulcers.

# Protocol for the comprehensive treatment of pressure ulcers

It must be emphasized that our protocol to prevent development of new pressure ulcers and promote the healing of existing ulcers must be initiated with the patient (or guardian) and the primary medical physician and bedside nurse. The protocol consists of the following:

- 1. Acknowledge that every patient with limited mobility is at risk for developing a sacral, ischial, trochanteric, or heel ulcer [26,27]
- 2. Daily assessment of the skin, particularly around the at-risk areas, including ischial, sacral, trochanteric, and heel areas [28,29]
- 3. Objective measurement of every wound by photography (at a minimum, weekly) and thorough documentation of the wound's progress with a graph [30], recording the wound area, depth, and region and degree of undermining
- 4. Immediate initiation of a treatment protocol upon recognition of a break in the skin [31]
- 5. Mechanical debridement of all nonviable tissue [32,33]
- 6. Effective wound-bed preparation and establishment of a moist wound-healing environment [31,34,35]
- 7. Aggressive nutritional supplementation of all malnourished/undernourished patients [36,37]
- 8. Pressure relief for the wound and other at-risk areas [38.39]
- 9. Elimination of all drainage and cellulitis [31]
- 10. Consideration of biological therapies for all patients with wounds not healing rapidly after initial treatment [40–42]
- 11. Physical therapy [31]
- 12. Palliative care

Acknowledge that every patient with limited mobility is at risk for developing a sacral, ischial, trochanteric, or heel ulcer

Early recognition and intervention are vital to successful treatment of pressure ulcers. Every patient at risk must have the skin around the trochanteric, sacral, ischial, and heel areas examined daily. Any break in the skin must be documented immediately and a treatment plan initiated directly. Together the primary care physician and wound-care specialist must establish a definitive and comprehensive treatment plan for healing the wound from the moment it is first detected. All clinicians caring for the patient must follow the established treatment plan to accomplish successful healing. Use of an interdisciplinary treatment approach that integrates physicians, social workers, physical therapists, and clinical nurses has been demonstrated to be most effective in treating these patients [43].

Daily assessment of the skin, particularly around the atrisk areas, including ischial, sacral, trochanteric, and heel areas

Bed- and wheelchair-bound patients are at greater risk of developing pressure ulcers and must be monitored daily, which includes the high-risk areas, that is, ischial, sacral, trochanteric, and heel. The patients also should be turned 2 to 3 times each day to relieve persistent pressure. In bed-bound patients, pressure ulcers can develop in <2 hours [44]. Therefore, daily evaluation and measurement are vital in preventing their progression.

Objective measurement of every wound (at a minimum, weekly) and thorough documentation of the wound's progress with a graph

As soon as an ulcer occurs, daily examination of the wound and thorough documentation of the wound's findings in the medical charts must be initiated. A full evaluation of the ulcer is mandatory; documentation of stage, length, width, depth, absence or presence of cellulitis, and amount and character of drainage must be performed at least once weekly [33]. A simple recording of measurements in the patient's chart is minimally acceptable, although planimetry measurements are optimal. These quantitative, objective measurements reduce the error associated with qualitative assessment and notation. A wound may "look good" and nevertheless fail to contract, epithelialize, or close in a timely manner. That wound also may be progressing toward osteomyelitis or may be the source of fever or sepsis.

Immediate initiation of a treatment protocol upon recognition of a break in the skin

Acknowledging that pressure ulcers cannot always be prevented is essential in establishing an accurate understanding of the problem. We now know that pressure ulcers can be treated easily and effectively if recognized and treated early. Many treatment modalities are available for pressure ulcers, including alternating air therapy, a method proved effective as a preventive measure. Hospitals may determine that owning these alternating air beds to use for

Table 2
Mandatory wound-bed preparation for pressure ulcers

- Removal of nonviable tissue
- Evaluation of pathologic findings (eg, granulation tissue, scar, gangrene, infection, fibrosis, tumor)
- Evaluation and treatment of deep culture: goal, to decrease bacterial count
- · Absence of cellulitis and elimination of odor
- Pressure relief and stimulation of blood flow (alternating air therapy)
- · Absence of drainage
- Stimulation of angiogenesis
- Stimulation of new collagen formation
- Stimulation of epithelialization
- Initiation of closure and contraction

routine treatment of bed-bound patients is economically advantageous [45].

#### Mechanical debridement of all nonviable tissue

For most wounds, simple sharp excision of superficial tissue, nonviable scar tissue, and infected tissue contribute to accelerating wound closure. Debridement stimulates healing by removing necrotic tissue that impedes healing and masks underlying fluid collections or abscesses. In the presence of necrotic tissue, wound healing is usually impossible. Moist necrotic tissue is yellow or gray; dry necrotic tissue is thick, hard, leathery, and black [46].

Debridement can be achieved using a variety of methods: sharp, mechanical, chemical, and autolytic. Sharp debridement with a scalpel is both the most effective and readily available treatment. To determine tissue viability and presence of infection (eg, scar versus granulation tissue), all tissue should be sent for pathologic analysis. Using a sterile technique, the remaining deep tissue should be sent for pathologic analysis and culture. If the deep tissue cultures are positive for the presence of bacteria and the wound is not healing (neither contracting nor epithelializing), further intervention is required, which generally entails additional mechanical debridement, use of antibiotics, or both. Surgical debridement of any area of undermining is mandatory. The wound margins should not be extended more than several millimeters into healthy tissue.

Effective wound-bed preparation and establishment of a moist wound-healing environment

Wound-bed preparation is considered adequate only after all scar tissue and infection are removed. Wound-bed preparation should be directed toward creating a moist woundhealing environment, while facilitating granulation tissue formation (ie, new collagen formation and angiogenesis) and decreasing bacterial count or load in the wound.

The goal of wound-bed preparation is to have well-vascularized granulation tissue without signs of local infection, which includes drainage, cellulitis, and odor (Table 2).

Three topical treatments shown to enhance the wound-bed preparation are (1) Iodosorb (Smith and Nephew, Hull, United Kingdom), an efficient antiseptic that does not inhibit the healing process [47]; (2) the nanocrystalline silverbased dressings, such as Acticoat (Smith and Nephew, Largo, FL), Actisorb Silver 220 (Johnson & Johnson, New Brunswick, NJ), and Acquacel Ag (Convatec, Princeton Junction, NJ) [48], which are reported to minimize the potential of fungal infection, thereby reducing some complications that delay wound healing [49], and (3) collagenase, which although designed as a chemical debriding agent, may also help prepare the wound bed and stimulate local granulation tissue.

Osteomyelitis merits special consideration. By definition, ulcers that penetrate to visible bone have osteomyelitis. In these cases, antibiotics should be administered before rather than after surgery.

Aggressive nutritional supplementation for all malnourished/undernourished patients

In addition to protecting healthy skin from damage, good nutritional status is essential for healing pressure ulcers. The patient's nutritional status should be evaluated thoroughly and managed by a specialist (an endocrinologist) as soon as the pressure ulcer is detected. A holistic assessment of nutrition must include glucose, vitamin, and protein levels. Diet must be adjusted to each individual patient's needs [50]. Therefore, if a patient is malnourished when he or she enters the hospital, a comprehensive regimen must be implemented immediately.

Blood tests and body-weight measurements are taken regularly to ensure maintenance of proper nutrition. Also, any patient whose albumin or prealbumin levels are not normal must have a documented treatment plan implemented. After patients leave the hospital (or their health provider's care), they should be educated to assess and maintain their own nutritional health.

## Pressure relief for the wound and other at-risk areas

Ultimately, the goal of tissue load management is to develop an environment that enhances the viability of soft tissues and promotes healing. In addition to the vigilant use of proper positioning techniques, support surfaces designed to decrease pressure, friction, and shear, while providing adequate levels of moisture and temperature to promote tissue health and growth, also should be used. After a break in the skin occurs, a pressure-relief system should be initiated. Using a low-pressure therapeutic mattress (eg, the alternating air mattress) may prove crucial in reducing the incidence of pressure ulcers. Such mattresses increase blood flow by reducing pressure. When using this mattress, the patient does not require continual shifts in position to avoid constant pressure on the area of the ulcer or other at-risk areas. Not only is it often impractical to advise bed-bound

patients to "stay off of a wound," but this also may precipitate new pressure ulcers by applying excess pressure to other at-risk areas.

Currently, it is not known which bed is "ideal." However, 2 factors—pressure relief and increasing blood flow—are important when determining the best bed surface. Selection of a bed surface is an integral component of a wound-healing regimen and a critical part of the woundhealing choice of interventions. In our experience, alternating air therapy has halted the progression of pressure ulcers. It increases blood flow, decreases pressure, and is usually comfortable for the patient. Pressure-relief beds play a major role in reducing overall costs by preventing pressureulcer progression. Currently, it is not possible to have a bed surface that prevents all pressure ulcers. Regardless of which type of bed surface is used, when a choice is made, it must be one that maximally decreases pressure and potentially increases regional blood flow. A bed that maximally relieves pressure is as mandatory for pressure ulcers as controlling glucose for a patient with diabetes mellitus.

# Elimination of all drainage and cellulitis

Cellulitis occurs when infection from the ulcer spreads to surrounding tissue; it is serious and frequently complicates pressure ulcers that are not treated effectively. All cellulitis must be eliminated by use of moist dressings, antibiotics, and surgery. Drainage, another potential sign of infection, must be eliminated. A successfully healed wound has neither cellulitis nor drainage.

Fungus around a wound is often the result of cellulitis. Fungus is easy to recognize and has a classic pattern. It should be treated with a topical antifungal agent. If no response is present (measured by objective improvement, ie, photographs) within 5 days, an oral antifungal should be added to the treatment regimen. An additional method to control fungus is to change the enteric feeds so they are better tolerated.

Consideration of biological therapies for all patients with wounds not healing rapidly after initial treatment

Growth factors have exhibited significant results in promoting wound healing. Platelet-derived growth factor—BB has proved to be effective with few side effects [51,52]. In addition, granulocyte/macrophage colony-stimulating factor (GM-CSF) can accelerate the healing of pressure ulcers [41]. GM-CSF has been particularly useful for stimulation of granulation tissue formation in treating deep ulcers. Apligraf (bilayered living human skin equivalent; Organogenesis, Inc, Canton, MA) consists of human keratinocytes and fibroblasts [53], and has proved to be effective in healing large surface wounds, including pressure ulcers [54]. Human skin equivalent supplies the wound with additional fibroblasts and keratinocytes, 2 cells that release growth

factors necessary for wound healing. These therapies assist in accelerating closure of pressure ulcers.

# Physical therapy

Physical therapy is important for all bed-bound and physically impaired patients, especially those with pressure ulcers. Physical therapy is important in (1) preventing contractions, (2) decreasing the chance of deep vein thrombosis, (3) decreasing respiratory complications, and (4) increasing mental acuity.

# Palliative care

Patients who receive palliative care are of special concern in the context of wound healing. There is a high incidence of pressure ulcers in the palliative-care setting. Contrary to the common belief that most pressure ulcers occur in the trochanteric area, the majority (79%) of pressure ulcers in palliative-care patients occur in the sacral area [55]. For patients undergoing palliative care, surgical treatment might not be appropriate, particularly in the homebound patient. In these palliative-care patients, therapy should be directed only toward relieving pain and halting pressure-ulcer progression. If the possibility of changing the patient's status from palliative to active care exists, comprehensive treatment must be initiated at that time.

#### Conclusion

Recognition that a chronic wound, by definition, has physiologic impairments to healing is significant in designing a treatment regimen. Initial recognition of a pressure ulcer should prompt immediate intervention. All bed-bound patients are at risk for developing pressure ulcers and should be examined daily. A common misconception is that bed-bound and chronically, critically ill patients can be treated effectively by use of only wet-to-dry dressings and a moist wound-healing environment. This theory is mistakenly considered "conservative therapy." Therapy for all patients must incorporate all aspects of this treatment protocol to achieve rapid, successful healing, as measured by wound contraction without cellulitis or drainage.

The risks associated with treating or not treating pressure ulcers must be clearly identified. After a collaborative treatment plan is developed, it can be presented to the patient or the patient's guardian. When discussing care, it is essential that the risks of nonhealing are explained and that all available options for healing are clarified. Only after this final discussion between the wound-healing specialist, physician, and patient occurs can a truly comprehensive plan be developed. If the patient is undergoing palliative care, the family should be informed that the pressure ulcer might likely be a source of pain and suffering if left untreated. If treatment for other illnesses is initiated for the palliative-

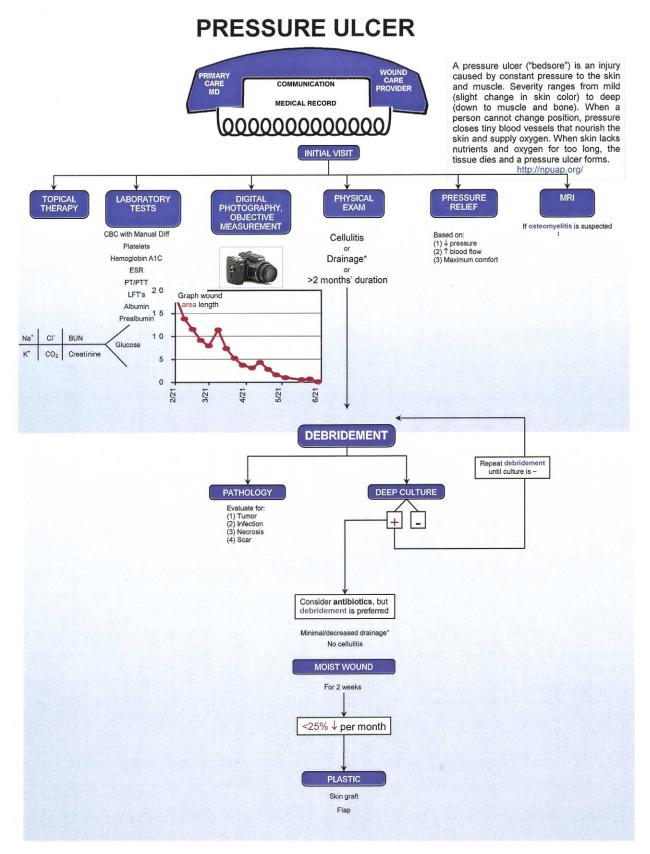


Fig. 2. Schematic representation of the pressure ulcer protocol. \* Drainage is often a sign of infection, in which case compression is not advisable. BUN = serum urea nitrogen; CBC = complete blood cell count; ESR = erythrocyte sedimentation rate; LFTs = liver function tests; MRI = magnetic resonance imaging; PT = prothrombin time; PTT = partial thromboplastin time.

care patient, comprehensive pressure ulcer treatment should be considered.

Pressure ulcers are chronic wounds from the moment they occur. These ulcers are primarily the products of a combination of pressure and decreased angiogenic response. Early intervention and comprehensive treatment should result in complete healing of ulcers that have not progressed to stage IV and have no osteomyelitis. Our paradigm is highly effective in achieving complete healing of these wounds (100% epithelialization and absence of drainage). When this protocol is followed, most pressure ulcers heal, and the consequent mortality, morbidity, and costs associated with progression of these ulcers decrease (Fig. 2).

#### References

- [1] Lyder CH. Pressure ulcer prevention and management. JAMA 2003; 289:223–226.
- [2] Barrois B, Allaert FA, Colin D. A survey of pressure sore prevalence in hospitals in the greater Paris region. J Wound Care 1995;4:234– 236
- [3] Baumgarten M, Margolis D, Berlin JA, Strom BL, Garino J, Kagan SH, Kavesh W, Carson JL. Risk factors for pressure ulcers among elderly hip fracture patients. Wound Repair Regen 2003;11:96–103.
- [4] Pearson A, Francis K, Hodgkinson B, Curry G. Prevalence and treatment of pressure ulcers in northern New South Wales. Aust J Rural Health 2000;8:103–110.
- [5] Meehan M. Multisite pressure ulcer prevalence survey. Decubitus 1990;3:14–17.
- [6] Bours GJ, Halfens RJ, Lubbers M, Haalboom JR. The development of a national registration form to measure the prevalence of pressure ulcers in The Netherlands. Ostomy Wound Manage 1999;45:28– 33.36–38.40.
- [7] Allman RM, Laprade CA, Noel LB, et al. Pressure sores among hospitalized patients. Ann Intern Med 1986;105:337–342.
- [8] Brandeis GH, Morris JN, Nash DJ, Lipsitz LA. The epidemiology and natural history of pressure ulcers in elderly nursing home residents. JAMA 1990;264:2905–2909.
- [9] Walter JS, Sacks J, Othman R, et al. A database of self-reported secondary medical problems among VA spinal cord injury patients: its role in clinical care and management. J Rehabil Res Dev 2002; 39:53–61.
- [10] Garber SL, Rintala DH. Pressure ulcers in veterans with spinal cord injury: a retrospective study. J Rehabil Res Dev 2003;40:433–41.
- [11] O'Brien SP, Gahtan V, Wind S, Kerstein MD. What is the paradigm: hospital or home health care for pressure ulcers? Am Surg 1999;65: 303–306.
- [12] Lazarus GS, Cooper DM, Knighton DR, et al. Definitions and guidelines for assessment of wounds and evaluation of healing. Arch Dermatol 1994;130:489–493.
- [13] Franks PJ, Winterberg H, Moffatt CJ. Health-related quality of life and pressure ulceration assessment in patients treated in the community. Wound Repair Regen 2002;10:133–140.
- [14] Capitano B, Leshem OA, Nightingale CH, Nicolau DP. Cost effect of managing methicillin-resistant *Staphylococcus aureus* in a long-term care facility. J Am Geriatr Soc 2003;51:10–16.
- [15] Dale MC, Burns A, Panter L, Morris J. Factors affecting survival of elderly nursing home residents. Int J Geriatr Psychiatry 2001;16:70– 76
- [16] Berlowitz DR, Brandeis GH, Anderson J, Du W, Brand H. Effect of pressure ulcers on the survival of long-term care residents. J Gerontol A Biol Sci Med Sci 1997;52:M106–M110.

- [17] Maklebust J. Pressure ulcer assessment. Clin Geriatr Med 1997;13: 455–481.
- [18] Ducker A. Pressure ulcers: assessment, prevention, and compliance. Case Manager 2002;13:61–65.
- [19] Brem HVB, Nierman D, et al. High morbidity and hospital costs of stage IV pressure ulcers [abstract]. Wound Repair Regen 2001;9.
- [20] Severens JL, Habraken JM, Duivenvoorden S, Frederiks CM. The cost of illness of pressure ulcers in The Netherlands. Adv Skin Wound Care 2002;15:72–77.
- [21] Xakellis GC, Frantz R. The cost of healing pressure ulcers across multiple health care settings. Adv Wound Care 1996;9:18–22.
- [22] Auerbach R, Auerbach W. Regional differences in the growth of normal and neoplastic cells. Science 1982;215:127–134.
- [23] Auerbach R, Morrissey LW, Kubai L, Sidky YA. Regional differences in tumor growth: studies of the vascular system. Int J Cancer 1978;22:40–46.
- [24] Kubai L, Auerbach R. Regional differences in the growth of skin transplants. Transplantation 1980;30:128–131.
- [25] Brem H, Tomic-Canic M, Tarnovskaya A, et al. Healing of elderly patients with diabetic foot ulcers, venous stasis ulcers, and pressure ulcers. Surg Technol Int 2003;11:161–167.
- [26] Keller BP, Wille J, van Ramshorst B, van der Werken C. Pressure ulcers in intensive care patients: a review of risks and prevention. Intensive Care Med 2002;28:1379–1388.
- [27] Salzberg CA, Byrne DW, Cayten CG, van Niewerburgh P, Murphy JG, Viehbeck M. A new pressure ulcer risk assessment scale for individuals with spinal cord injury. Am J Phys Med Rehabil 1996; 75:96–104.
- [28] Wong VK, Stotts NA. Physiology and prevention of heel ulcers: the state of science. J Wound Ostomy Continence Nurs 2003;30:191– 198.
- [29] Ayello E. Teaching the assessment of patients with pressure ulcers. Decubitus 1992;5:53–54.
- [30] Goldman RJ, Salcido R. More than one way to measure a wound: an overview of tools and techniques. Adv Skin Wound Care 2002;15: 236–243.
- [31] Brem H. Specific paradigm for wound bed preparation in chronic wounds. In: Cherry GW, Harding KG, Ryan TJ, eds, for the European Tissue Repair Society. Wound Bed Preparation. London: RSM Press, 2000:33–39.
- [32] Longe RL. Current concepts in clinical therapeutics: pressure sores. Clin Pharm 1986;5:669–681.
- [33] Brem H, Nierman DM, Nelson JE. Pressure ulcers in the chronically critically ill patient. Crit Care Clin 2002;18:683–694.
- [34] Schultz GS, Sibbald RG, Falanga V, et al. Wound bed preparation: a systematic approach to wound management. Wound Repair Regen 2003;11(suppl 1):S1–S28.
- [35] Romanelli M, Mastronicola D. The role of wound-bed preparation in managing chronic pressure ulcers. J Wound Care 2002;11:305–310.
- [36] Lewis M, Pearson A, Ward C. Pressure ulcer prevention and treatment: transforming research findings into consensus based clinical guidelines. Int J Nurs Pract 2003;9:92–102.
- [37] Strauss EA, Margolis DJ. Malnutrition in patients with pressure ulcers: morbidity, mortality, and clinically practical assessments. Adv Wound Care 1996;9:37–40.
- [38] Cullum N, Deeks J, Sheldon TA, Song F, Fletcher AW. Beds, mattresses and cushions for pressure sore prevention and treatment. Cochrane Database Syst Rev 2000;(3):CD001735.
- [39] Armstrong D, Bortz P. An integrative review of pressure relief in surgical patients. AORN J 2001;73:645–657.
- [40] Robson MC, Hill DP, Smith PD, et al. Sequential cytokine therapy for pressure ulcers: clinical and mechanistic response. Ann Surg 2000; 231:600-611.
- [41] Robson MC, Phillips LG, Lawrence WT, et al. The safety and effect of topically applied recombinant basic fibroblast growth factor on the healing of chronic pressure sores. Ann Surg 1992;216:401–408.

- [42] Payne WG, Ochs DE, Meltzer DD, et al. Long-term outcome study of growth factor-treated pressure ulcers. Am J Surg 2001;181:81–86.
- [43] Carasa M, Nespoli G. Nursing the chronically critically ill patient. Crit Care Clin 2002;18:493–507.
- [44] Reuler JB, Cooney TG. The pressure sore: pathophysiology and principles of management. Ann Intern Med 1981;94:661–666.
- [45] Lyder CH. Pressure ulcer prevention and management. Annu Rev Nurs Res 2002;20:35–61.
- [46] Maklebust J, Sieggreen M. Pressure Ulcer: Guidelines for Prevention and Management, 3rd ed. Springhouse, PA, 2001.
- [47] Johnson A. A combative healer with no ill effect: Iodosorb in the treatment of infected wounds. Prof Nurse 1991;7:60-64.
- [48] Thomas S, McCubbin P. A comparison of the antimicrobial effects of four silver-containing dressings on three organisms. J Wound Care 2003;12:101–107.
- [49] Wright JB, Lam K, Hansen D, Burrell RE. Efficacy of topical silver against fungal burn wound pathogens. Am J Infect Control 1999;27: 344–350.

- [50] Mechanick JI, Brett EM. Nutrition support of the chronically critically ill patient. Crit Care Clin 2002;18:597–618.
- [51] Rees RS, Robson MC, Smiell JM, Perry BH. Becaplermin gel in the treatment of pressure ulcers: a phase II randomized, double-blind, placebo-controlled study. Wound Repair Regen 1999;7:141–147.
- [52] Kallianinen LK, Hirshberg J, Marchant B, Rees RS. Role of plateletderived growth factor as an adjunct to surgery in the management of pressure ulcers. Plast Reconstr Surg 2000;106:1243–1248.
- [53] Brem H, Young J, Tomic-Canic M, Isaacs C, Ehrlich HP. Clinical efficacy and mechanism of bilayered living human skin equivalent (HSE) in treatment of diabetic foot ulcers. Surg Technol Int 2003; 11:23-31
- [54] Brem H, Balledux J, Bloom T, Kerstein MD, Hollier L. Healing of diabetic foot ulcers and pressure ulcers with human skin equivalent: a new paradigm in wound healing. Arch Surg 2000;135:627– 634
- [55] Galvin J. An audit of pressure ulcer incidence in a palliative care setting. Int J Palliat Nurs 2002;8:214-221.