Clinical Approach to Wounds: Débridement and Wound Bed Preparation Including the Use of Dressings and Wound-Healing Adjuvants

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Summary: This is a clinical review of current techniques in wound bed preparation found to be effective in assisting the wound-healing process. The process begins with the identification of a correct diagnosis of the wound's etiology and continues with optimizing the patient's medical condition, including blood flow to the wound site. Débridement as the basis of most wound-healing strategies is then emphasized. Various débridement techniques, including surgery, topical agents, and biosurgery, are thoroughly discussed and illustrated. Wound dressings, including the use of negative pressure wound therapy, are then reviewed. To properly determine the timing of advance therapeutic intervention, the wound-healing progress needs to be monitored carefully with weekly measurements. A reduction in wound area of 10 to 15 percent per week represents normal healing and does not mandate a change in the current wound-healing strategy. However, if this level of wound area reduction is not met consistently on a weekly basis, then alternative healing interventions should be considered. There is a growing body of evidence that can provide guidance on the appropriate use of such adjuvants in the problem wound. Several adjuvants are discussed, including growth factor, bioengineered tissues, and hyperbaric medicine. (*Plast. Reconstr. Surg.* 117 (Suppl.): 72S, 2006.)

The goal of treating any type of wound is to create an environment that is conducive to normal and timely healing. An *acute wound* is defined as a recent wound that has yet to progress through the sequential stages of wound healing. A *chronic wound* is a wound that is arrested in one of the wound-healing stages (usually the inflammatory stage) and cannot progress further. The purpose of this article is to discuss clinically relevant *local* strategies to facilitate normal wound healing. The focus will be on the role of débridement and modern wound-healing adjuncts, such as negative pressure wound therapy, topical growth factors, bioengineered tissue, and hyperbaric oxygen. Throughout this discussion, it is usually assumed that the etiology of the wound has been correctly diagnosed, that the local blood flow to the area has been optimized, and that medical and nutritional abnormalities have been corrected.

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Débriding a wound is defined as removing necrotic tissue, foreign material, and bacteria from an acute or chronic wound. Necrotic tissue, foreign material, and bacteria impede the body's attempt to heal by producing or stimulating the production of metalloproteases that overwhelm the local wound-healing process. In this process, the building blocks (chemotactants, growth factors, mitogens, and so on) necessary for normal wound healing are either rendered inert or destroyed. This hostile environment allows bacteria to proliferate and further colonize the wound as they protect themselves and their colonies from potential destruction within a biofilm construct. The bacteria produce their own wound-inhibiting enzymes and, more significantly, consume many of the scarce local resources (oxygen, nutrition, and building blocks) that are necessary for wound healing.

Débriding the acute wound removes damaged tissue or foreign material as well as bacteria that might inhibit healing. This enables the wound to go through the normal wound-healing phases, assuming that systemic and local factors are functioning normally. Aggressive débridement of a chronic wound converts the entire wound base

into an acute wound, so that it can progress through the normal phases of wound healing.

THE IMPORTANCE OF DÉBRIDEMENT

Infection of a wound site alters the normal healing process by disrupting and prolonging the inflammatory phase.[1] This inhibits the ability of macrophages to direct the repair process, including débridement, formation of granulation tissue, and neovascularization. Clinically, the bacterial status of a wound can be assessed by quantitative counts. A well-vascularized wound with a bacterial count of less than 10^5 bacteria per gram of tissue should go on to heal by secondary intention or successfully accept a skin graft.[2–4] If the bacterial concentration is higher, the wound's inflammatory response to the local bacteria can overwhelm local wound-healing efforts and prevent a skin graft from adhering to and being revascularized by the underlying bed. If it is allowed to persist unchecked, a superficial infection can potentially become systemic and lead to sepsis.[5] Aggressive removal of all necrotic, infected, and nonviable tissue prevents the establishment of a protease-rich environment that allows bacteria to proliferate in the wound base. The application of topical antibiotics, such as silver sulfadiazine, mafenide acetate, and silver nitrate, has proved to be a useful adjunct to help lower the bacterial count. [6,7] The combination of débridement to a viable tissue base and application of topical antibiotics is currently the mainstay of successful burn wound coverage.

Steed et al. reviewed the data regarding platelet-derived growth factor's effect on the healing of chronic diabetic wounds.[8] They observed that wounds healed more successfully when the wound débridement was performed weekly rather than more sporadically. The success rate of various clinical sites in the platelet-derived growth factor study was significantly correlated to the frequency of débridement. The most likely reason is that frequent débridements regularly remove inhibitors of wound healing (metalloproteases, including the collagenases matrix metalloproteinase 1 and 8^9 and elastases) and allow growth factors to function more effectively.[10]

The importance of removing the local inhibitory wound-healing factors may be one of the factors by which negative pressure wound therapy can successfully convert chronic wounds to healthy healing wounds.[11] The suction applied by the device to the surface of the wound decreases wound edema and prevents a build-up of proteases and bacteria. The end result is a decrease in the bacterial count and rapid formation of healthy granulation tissue.[12]

ASSESSING A WOUND BEFORE DÉBRIDEMENT

Before considering whether to débride a wound, one has to determine the wound's etiology, previously administered wound therapies, and the patient's medical condition. A thorough patient history should be obtained from the patient, family, friends, emergency medical technicians, and/or referring doctor to help determine the wound's etiology. The origin and age of the wound should be determined. If the wound is traumatic in origin, it should be defined in terms of high impact, low impact, repetitive, temperature related, caustic, radiation induced, type of bite, presence of drug abuse, and so on. The patient's tetanus immunization status should be obtained, and the patient should be re-inoculated if revaccination is indicated. In chronic wounds, the age of the wound is important because longstanding wounds can be malignant (Marjolin's ulcer). Previous topical therapy to the wound should be delineated, because certain topical agents can contribute to the wound's chronicity[13] (e.g., caustic agents such as hydrogen peroxide, 10% iodine, Dakin's solution, and so on) (Fig. 1).

A careful medical history should be obtained to evaluate the most likely disease states that directly affect wound healing. Attention should be focused on diseases that may negatively affect arterial inflow to and venous outflow from the wound. Close attention should be paid to the immune system, hematological system, and to nutrition, all of which can affect wound healing. The presence of autoimmune diseases (such as rheumatoid arthritis, pyoderma gangrenosum, systemic lupus erythematosus, scleroderma, and so on) may cause inflammatory wounds that initially need medical management rather than surgical care. Optimizing these wound types with medical management first will allow the wounds to undergo the normal stages of healing. It should be noted that the medications used to treat autoimmune diseases (i.e., steroids or chemotherapy) can also contribute to poor wound healing. Diseases that affect the neurological system (e.g., diabetes, paraplegia, spina bifida, and multiple sclerosis) blunt the normal response to trauma as well as wound healing. The nutritional status also affects wound healing and should be assessed (optimal is albumin >3.0 g/dl and/or total lymphocyte count greater than 1500). In persons with diabetes, the tight control of blood glucose levels

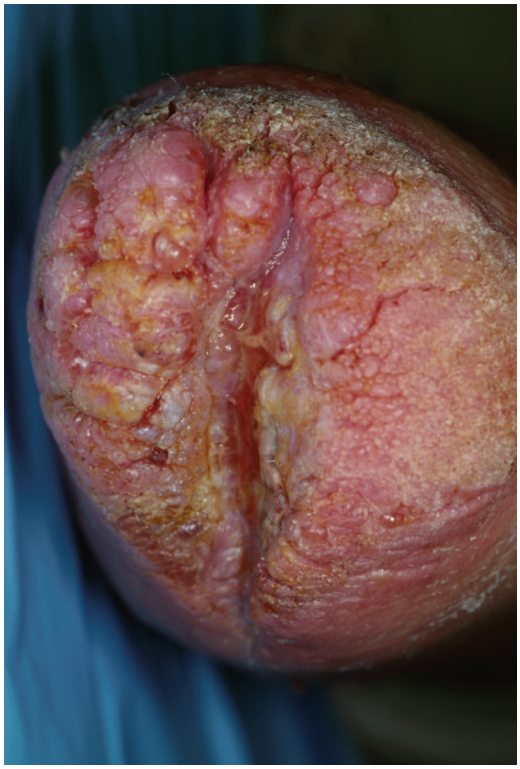

Fig. 1. The chronicity of wounds can be perpetuated by applying a caustic agent to the wound surface. Hydrogen peroxide, alcohol, 10% iodine, and so on all negatively affect the healing process. This stump was treated with hydrogen peroxide for 1 year and never healed.

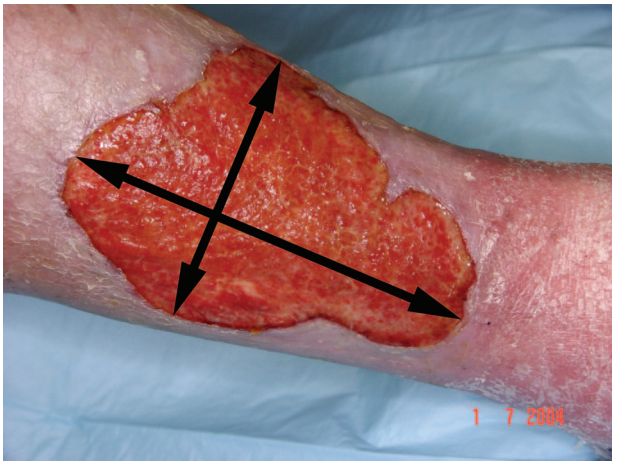

Fig. 2. The wound area is crudely determined by measuring the longest horizontal and vertical axes of the wound that are perpendicular to one another. The product is then recorded. Then the depth of the wound and the type of tissue exposed at the base of the wound are recorded.

is critical in optimizing the body's ability to fight infection and heal. Smoking significantly decreases local cutaneous flow and should be documented and addressed with the patient. Finally, a complete list of medications and drug allergies should be obtained. Given the complexity of various diseases affecting the healing process, multiple medical specialists may be called in to assist in the patient's medical management and help optimize their medical condition, so that the wound has a better chance of healing.

The wound should then be assessed carefully by measuring its size and depth. The area is determined by multiplying the length and width along the two longest axes perpendicular to one another (Fig. 2). An alternative is to use a commercial wound-measuring device that determines the exact wound area by tracing its perimeter. The depth and type of exposed tissue (dermis, subcutaneous tissue, fascia, muscle, and/or bone) should then be determined. The wound should be photographed and referenced with patient identification data and a ruler. If cellulitis is present, the border of the erythema should be delineated (Fig. 3). The physician can then determine before the culture results are available whether the initially prescribed antibiotics and/or initial débridement is successfully addressing the infection. If the erythema has extended beyond the inked boundary, either the antibiotics are inadequate or the wound has been inadequately débrided.

It is important not to confuse cellulitis with dependent rubor (Fig. 4, *above*). With dependent rubor, inflammation is absent and the skin has visible wrinkling. If the erythema present in an extremity disappears when it is elevated above the level of the heart, then the erythema is due to dependent rubor. If the erythema persists despite elevation, the wound has surrounding cellulitis and needs antibiotic treatment with or without débridement. Dependent rubor can also be seen at a postoperative site and should not be confused with postoperative cellulitis (Fig. 4, *below*).

The depth of the wound should be carefully assessed for tendon, joint, or bone involvement. A metallic probe (Fig. 5) can be used to assist in evaluating the depth of the wound. If the probe touches bone, there is an 85 percent chance that osteomyelitis[14] is present and a radiograph should be obtained. It is important to remember that it can take up to 3 weeks for osteomyelitis to be visible on a radiograph.[15] Magnetic resonance imaging is considered the accepted standard in diagnosing osteomyelitis in diabetic foot ulcerations. However, both magnetic resonance imaging and nuclear scans are expensive and unnecessary if the bone is going to be directly eval-

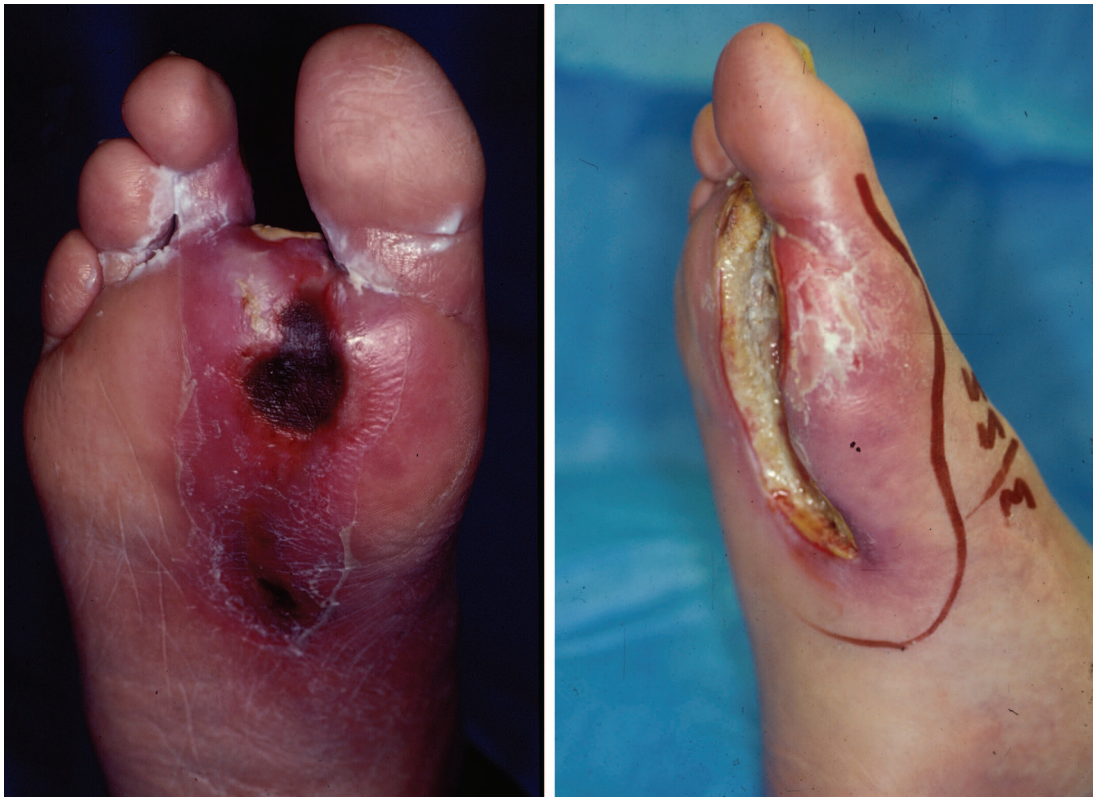

Fig. 3. A gangrenous forefoot with surrounding cellulitis (*left*) is initially débrided to viable tissue. The border of the erythema around the wound is then delineated with indelible ink (*right*). The time and date are likewise inscribed. The wound is then checked 4 to 6 hours later. If the erythema recedes, then the débridement and antibiotics chosen were appropriate initial treatment. If the erythema progresses beyond the border, then further débridement is necessary and/or the antibiotics need to be changed.

uated during débridement. These studies are useful if the extent of osteomyelitis in the suspected bone is unclear or if there is suspicion that other bones may be involved. If tendon is involved, the infection is very likely to have tracked along its sheath. The tendon sheath should be checked for bogginess and milked toward the open wound to assess whether there is purulence. If pus appears, then that tendon sheath will have to be opened along the infected track. If the suspicion is strong that a distal infection has spread proximally, the proximal areas where the tendon sheaths are readily accessible should be checked (i.e., dorsal or volar wrist, extensor retinaculum, tarsal tunnel, and so on). This can be done with a simple needle aspiration or the strategic placement of a small incision and spreading with a straight clamp to the tendon sheath.

The blood flow to the area should then be evaluated by palpation and/or handheld Doppler[16] (see "Wound Healing," by Broughton et al., in this issue). A triphasic Doppler signal indicates normal blood flow, a biphasic signal indicates adequate blood flow, and a monophasic signal warrants further investigation. If the quality of flow is questionable, a formal noninvasive arterial Doppler evaluation has to be performed. If the flow is inadequate, the patient should then be referred to a vascular surgeon who *specializes* in endovascular techniques and in distal revascularizations. Débridement should be delayed in a stable wound with dry gangrene and inadequate blood flow, until blood flow has been corrected (Fig. 6, *above, left*). Premature débridement of a devascularized wound may cause future loss of potentially salvageable tissue. However, immediate débridement is called for when wet gangrene, ascending cellulitis from a necrotic wound, or necrotizing fasciitis are present (Fig. 6, *above, right*, and *below*). Revascularization should follow as soon as the infection is under control.

Sensation and motor function must also be assessed. A careful nerve examination is crucial when ruling out compartment syndrome. In diabetic patients or those with neurological disorders, the neurological examination can help ex-

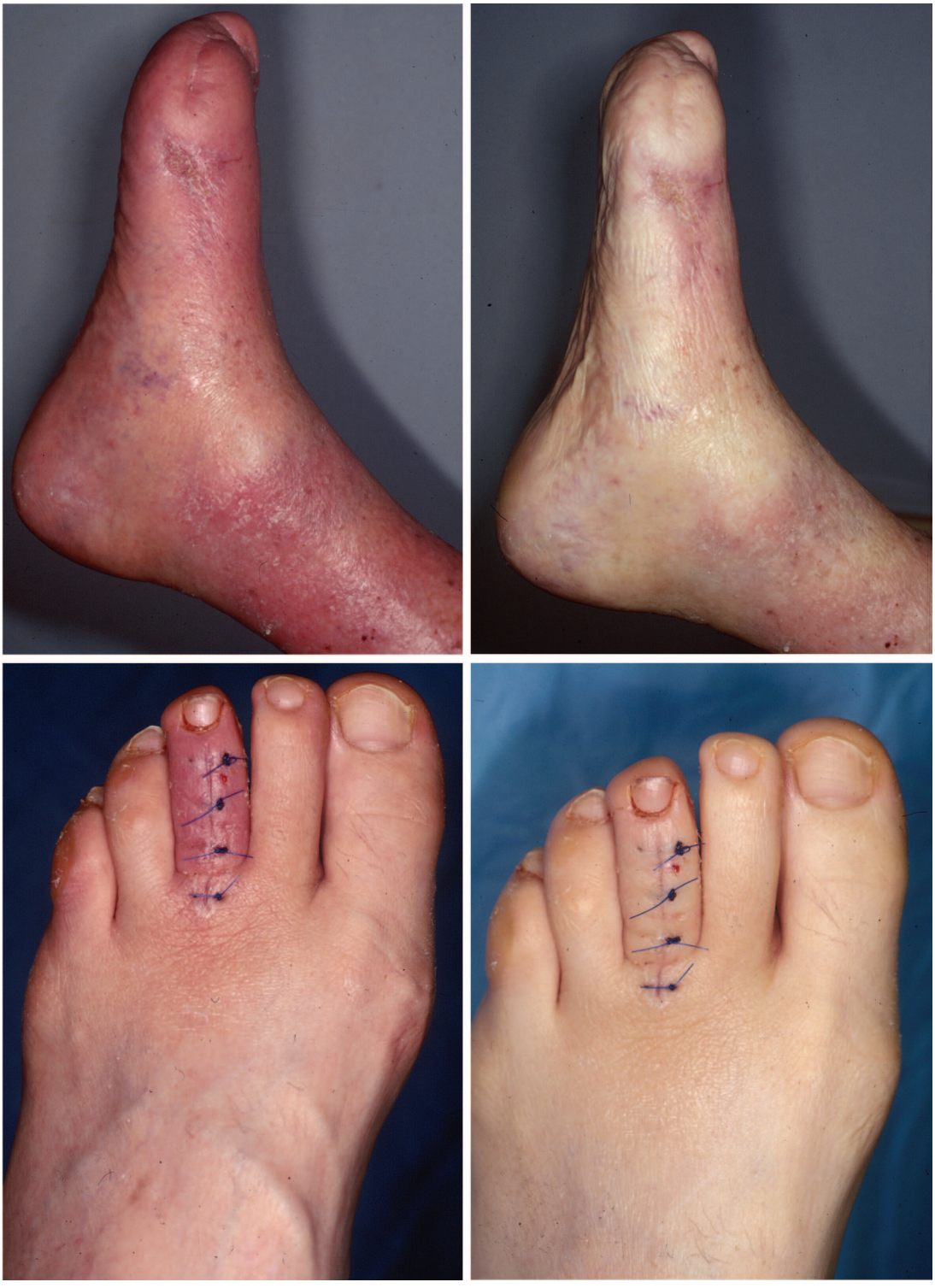

Fig. 4. An ischemic foot in a dependent position turns red and can be confused with cellulitis (*above, left*). The foot is then elevated above the level of the heart. If the erythema disappears (*above, right*), then it was due to dependent rubor rather than cellulitis. If it persists, then it is due to cellulitis and needs immediate treatment. The same erythema occurs in a freshly operated site. Note that the skin edges along the incision are wrinkled, which is consistent with dependent rubor (*below, left*). Elevation of the foot above the heart confirms the diagnosis (*below, right*).

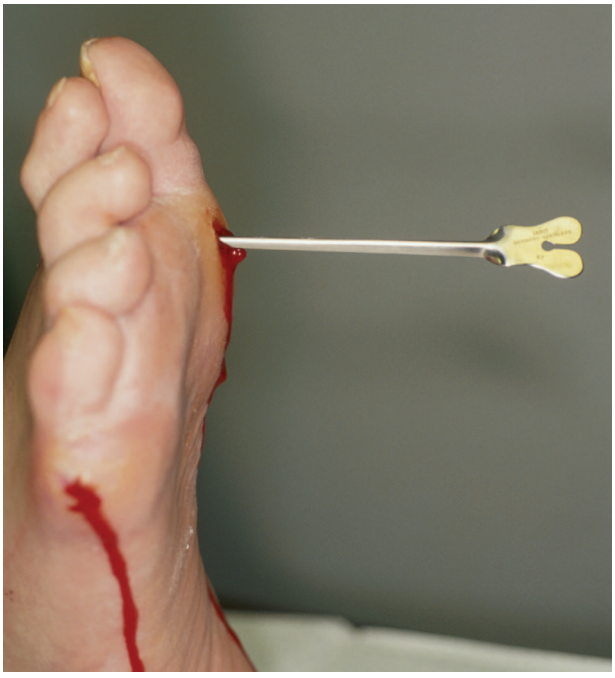

Fig. 5. A metal probe can be very useful for determining whether bone lies at the base of the wound. If bone is palpated, then there is an 85 percent chance that osteomyelitis is present.

plain whether neuropathy contributed to the wound's etiology and, if so, help in mapping out strategies to prevent recurrences. Lack of protective sensation can be established when the patient is unable to feel 10 g of pressure applied by a 5.07 Semmes-Weinstein filament (Fig. 7).[17,18] This sensory loss impairs patients from realizing damage that occurs due to excessive local pressure from prolonged decubitus position; tight shoes, clothes, or dressings; biomechanical abnormalities; or the presence of foreign bodies. The repetitive trauma of normal ambulation (on average, a person takes 10,000 steps a day) in neuropathic patients with biomechanical abnormalities leads to ulceration[19] because of high focal plantar pressures during gait.

Chronic hyperglycemia enables glycosylation of collagen with subsequent loss of elasticity in connective tissues.[20] An example is the glycosylation of the Achilles tendon, which destroys its flexibility and leads to an inability to dorsiflex the foot beyond neutral. This loss of motion places an excessive amount of pressure during the push-off phase of gait both at the arch/midfoot and underneath the metatarsal heads. The excess pressure at the midfoot can lead to Charcot collapse, while at the forefoot it can lead to ulceration at the plantar metatarsal heads. This problem is worsened in the concomitant neuropathic patient with hypesthesia at the midfoot or forefoot. Open or percutaneous release of the Achilles tendon[21,22] decreases forefoot pressure in the equinovarus foot during gait and can yield rapid healing of plantar forefoot ulcers (Fig. 8). In addition, the weakened triceps surae muscle decreases the recurrence of ulceration over the long term.[23] Correction of underlying biomechanical abnormalities, as well as treatment of the underlying medical conditions, is as important as débridement and wound care in the overall treatment plan.

DÉBRIDEMENT

The most important surgical step in treating any wound is to perform adequate débridement to remove all foreign material and unhealthy or nonviable tissue until the wound edges and base consist only of normal and healthy tissue. Only an *atraumatic* surgical technique[24] (sharp dissection, skin hooks, bipolar cautery, and so on) should be used to avoid damaging the underlying healthy tissue (Fig. 9). This tissue will become the basis for the wound-healing process to progress normally. Damaging it by crushing or burning may establish a nidus for bacteria to proliferate. This becomes even more apparent when dealing with the severely immunocompromised patient with poor blood flow (i.e., the renal failure diabetic patient with peripheral vascular disease).

The goal of surgical débridement is to excise the wound until only normal, soft, well-vascularized tissue remains. Although a tourniquet is placed on patients without ischemic disease as a precautionary measure, we prefer to débride the wound without an inflated tourniquet, so that the quality of bleeding at the débrided wound edges can be continually assessed. Bleeding can usually be stopped with gentle pressure with or without topical coagulants. Pinpoint cautery or suture ligation may be necessary. An acute wound has to be trimmed of all questionably viable tissue and foreign material, so that it can either progress through the normal healing phases or be closed safely. A chronic wound has to be converted by débridement to an acute wound, so that it can proceed through the normal healing phases. Deep tissue cultures should always be analyzed for pathogenic bacteria and to obtain sensitivities to potential therapeutic agents. In addition, the débrided tissue should be sent for pathologic analysis for a specific diagnosis of osteomyelitis, vasculitis, or cancer.

Inadequate débridement results from concerns about how to close and/or reconstruct the

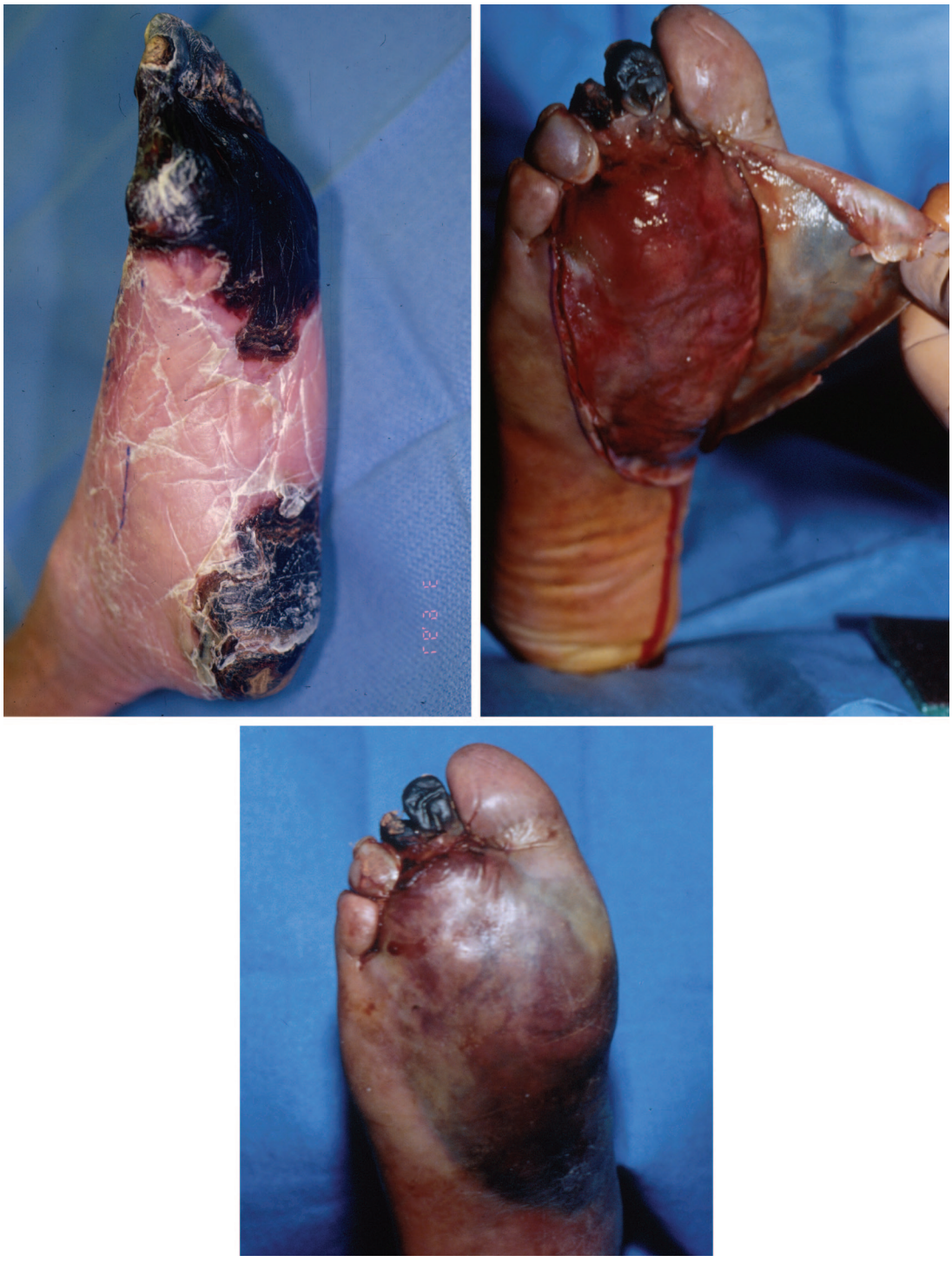

Fig. 6. A patient with dry gangrene and no cellulitis should be evaluated by the vascular surgeon and revascularized before débridement to save a maximal amount of tissue (*above, left*). However, if there is wet gangrene, surrounding cellulitis from a necrotic wound base, or necrotizing fasciitis, the wound should be débrided immediately (*above, right*, and *below*).

resultant defect. Thus, it is important to have at least one of the physicians on the multidisciplinary wound team be familiar with modern wound care techniques, negative pressure wound therapy, topical growth factor, bioengineered tissues, reconstructive wound closure techniques (skin graft,

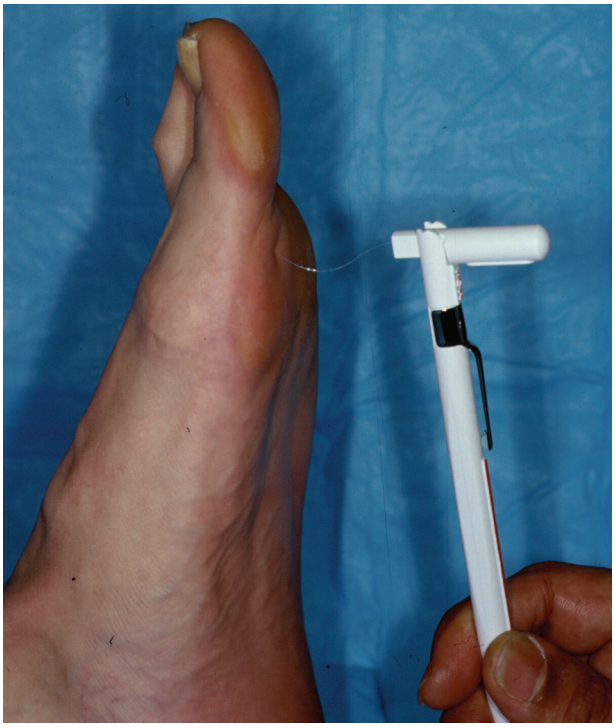

Fig. 7. The use of a 5.07 Semmes-Weinstein monofilament (equivalent to 10 g of pressure) on the various neurosomes of the foot is a simple way to assess whether sufficient protective sensation is present. If the patient cannot feel the filament when sufficient pressure is applied to bend it, then he or she is at risk for breakdown and has to alter the activities of daily living to guard against that eventuality.

local flaps, pedicled flaps, and microsurgical free flaps), and/or hyperbaric oxygen treatments. Most wounds can be closed by secondary intention, delayed primary closure, or skin graft coverage and do not require sophisticated plastic surgery reconstruction techniques. The advent of negative pressure wound therapy has, in large part, reduced the concerns about wound closure. The pressure device can provide rapid formation of granulation tissue, and its ability to decrease edema renders the wound a better candidate for simple wound closure techniques.[25] The subsequent wound can often be closed primarily or skin grafted instead of covered with a pedicled or microsurgical free flap.

For the sensate patient, a regional block with lidocaine allows the health professional to débride aggressively in the office under most circumstances. The wound should be débrided in the operating room if the wound cannot be adequately anesthetized with a regional block or if the débridement will lead to bleeding that may be difficult to control.

THE NECESSARY SURGICAL TOOLS AND TECHNIQUES OF DÉBRIDEMENT

The basic tools of surgical débridement used in an *office* include pickups, blades, scissors, curettes, and rongeurs. These should be surgical tools and not disposable suture removal kit tools, which are dull and cannot grasp or cut tissue adequately and as a result may damage healthy tissue. The pickups should have teeth, so that tissue to be excised can be grasped more easily without traumatizing additional tissue. A no. 15 blade is used for dissection around bone, while a no. 10 or 20 blade is used on soft tissue to slice thin layer after thin layer until healthy tissue is reached (Fig. 10). It is frequently necessary to change surgical blades, because they dull quickly. Strong sharp scissors (e.g., curved Mayo scissors) work well for dissecting eschar and dead tissue. Curettes with sharp edges are very useful in removing the proteinaceous coagulum that accumulates; the coagulum contains proteases and bacteria that inhibit healing (Fig. 11). Rongeurs are useful for removing hard-to-reach indurated soft tissue and for débriding bone.

Many surgical débridement tools in the *operating room* are found in the orthopedic trays. A Cobb elevator, with its long lever arm and sharp spoon-size tip, is useful for exposing bone. McElroy curettes (large curettes used to ream out the inside of the femur) are very useful in débriding large areas of chronic granulation tissue and deep cavities. Rongeurs are very useful in biting off indurated soft tissue in narrow spaces that are difficult to reach with a knife or scissor. They are also useful in débriding or biopsying bone, although great care has to be taken to avoid shattering the proximal bone. Rongeurs should be double action and include narrow and wide duckbills, as well as narrow and wide straights. A nitrogen-driven or electrical sagittal saw is useful for serially sawing off bone slices until normal cortex and marrow is reached. Cutting burrs and rasps are likewise useful in the fine débridement of the bone surface to reach the telltale punctate bleeding at the freshened bone surface (paprika sign).

When débridement is complete, it is important to cleanse the wound with a pulsed lavage system.[26] The pressure from the pulsating liquid is very effective in getting rid of any loose debris, tissue, and bacteria. When dealing with an extremity, it is helpful to place it in an isolation bag before pulse-evacuating the wound, to avoid contaminating the rest of the operating room field with the spray (Fig. 12). The irrigation solution

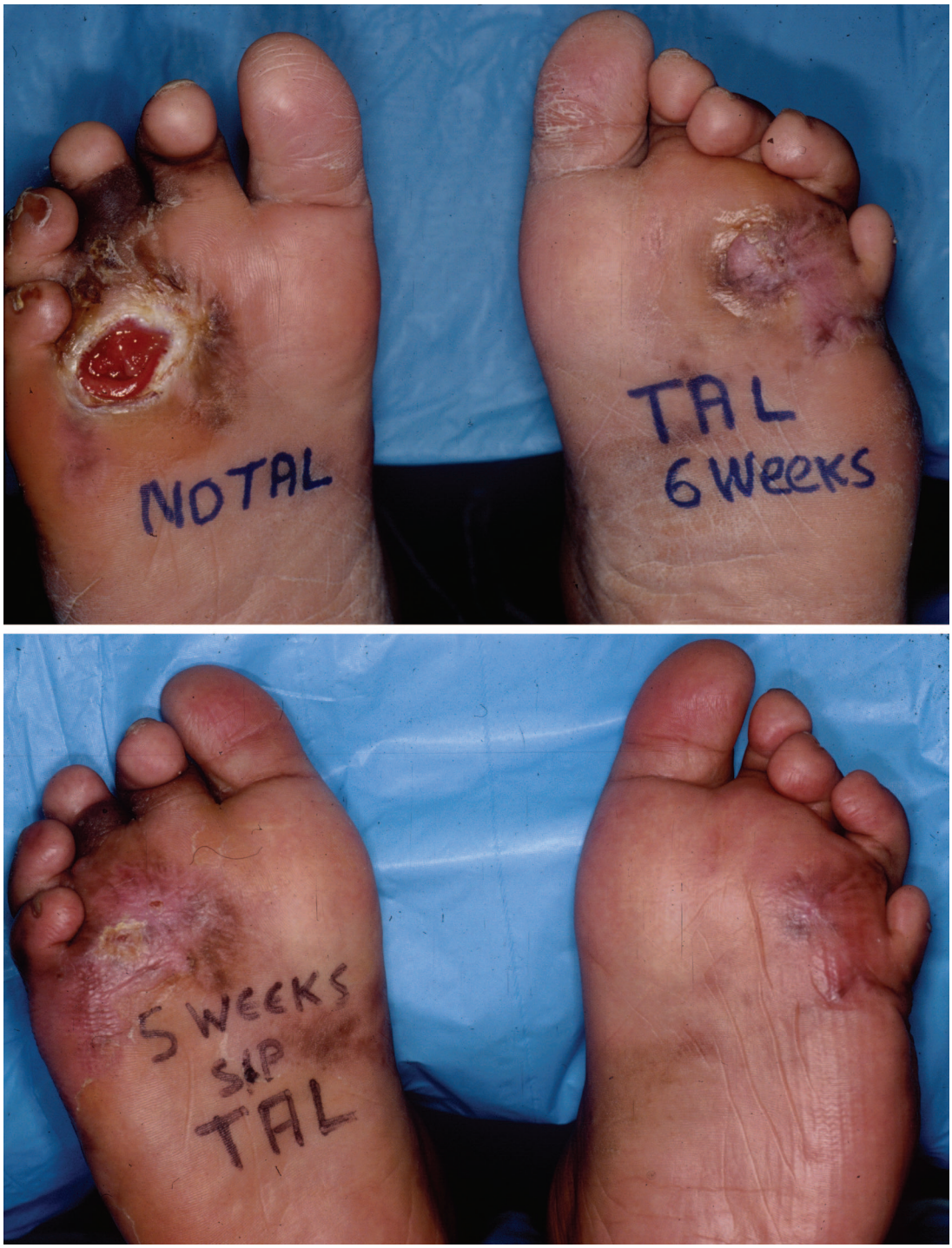

Fig. 8. A 39-year-old obese diabetic patient had bilateral lateral plantar metatarsal ulcers secondary to equinovarus deformity (*above*). Both the gastrocnemius and soleus portions of the Achilles tendon were tight. The left Achilles was released percutaneously, and the left foot healed in 6 weeks with conservative wound care of the ulcer (*below*). The right forefoot ulcer healed similarly within 5 weeks after Achilles tendon release. Correcting the biomechanical abnormality was all that was required for healing to occur. *TAL*, Achilles tendon lengthening.

should be normal saline without added antibiotics, as there has been no proven benefit to adding antibiotics to the saline used to lavage the wound. When pulse-lavaging a traumatic wound, it is important to first tag any important structures (nerve and tendon ends) with monofilament suture, be-

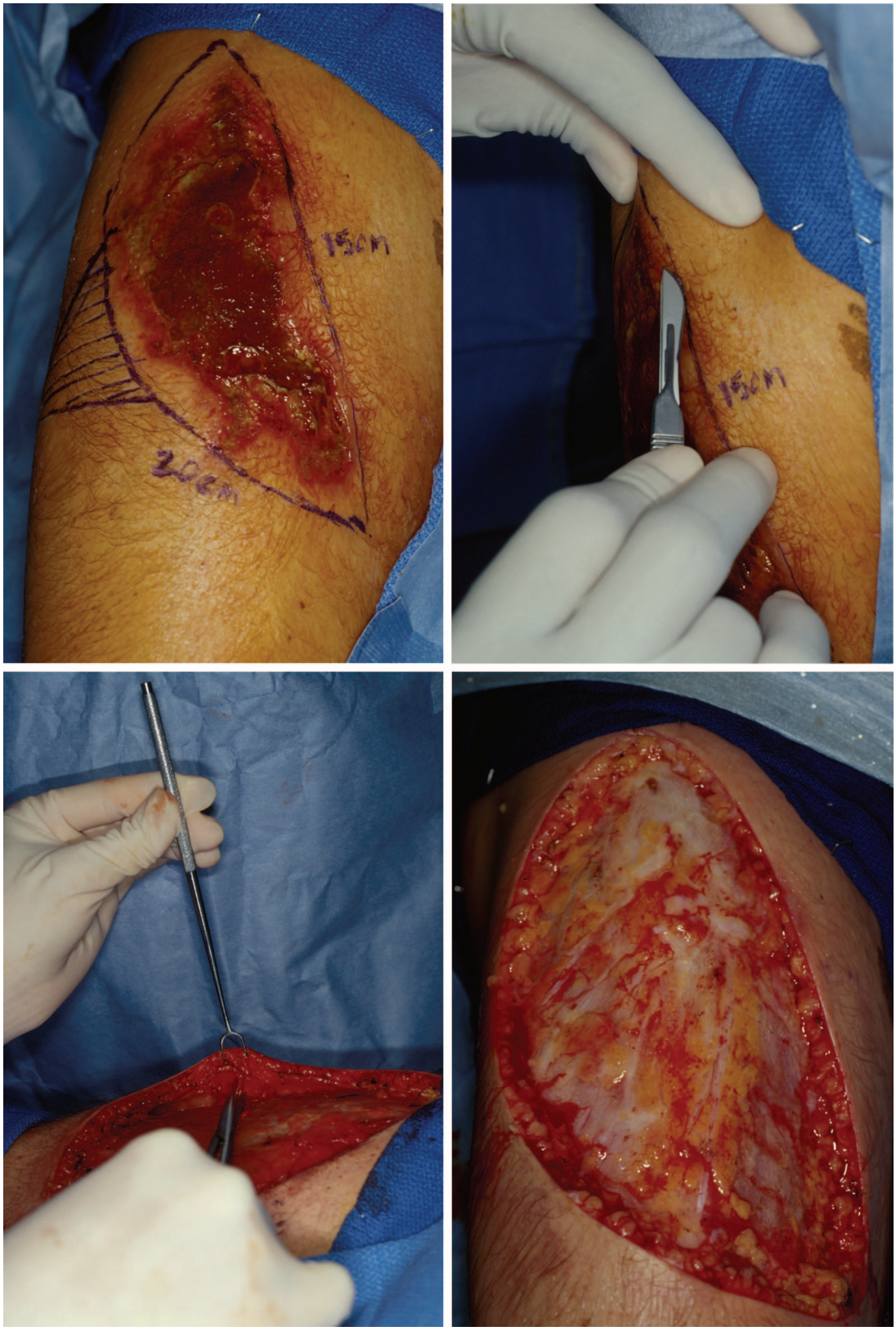

Fig. 9. (*Above, left*) A chronic, nonhealing wound on the thigh of a steroid-dependent diabetic patient with renal failure. Thorough débridement to healthy bleeding tissue both at the wound edges and base was required to convert this wound to an acute wound, so that it can go on to heal (*below, right*). The key in débridement is to avoid damaging the residual tissue by using excellent atraumatic surgical techniques. This means using skin hooks for retraction (*below, left*) rather than crushing forceps, and sharp dissection with a knife (*above, right*) rather than cautery to minimize damage to the tissue left behind.

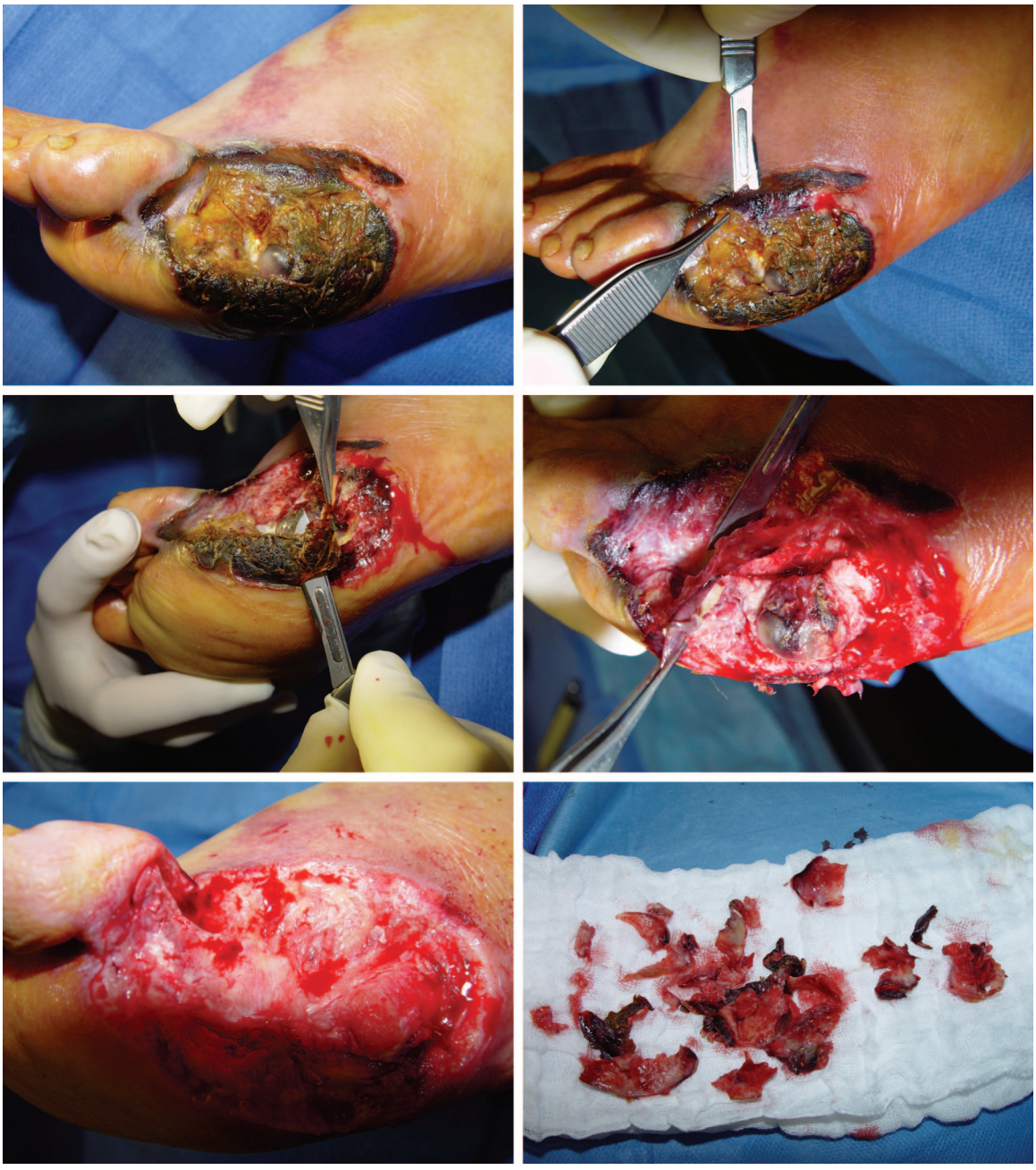

Fig. 10. (*Above, left*) A diabetic patient presented with wet gangrene of the medial forefoot. (*Above, right*, and *center, left and right*) A no. 10 blade was used in a sawing motion, cutting thin slice after thin slice, until viable and healthy-appearing tissue was reached (*below, left*). The blade may need to be changed frequently because it can quickly become dull. Note the many small slices of tissue are required to adequately débride the wound (*below, right*).

cause they may difficult to identify, as the surrounding structures tend to swell during the process.

Another surgical débriding tool is the Versajet, a hydrosurgical water knife (Smith & Nephew, Cambridge, England).[27] Its advantages are that one can very accurately control the depth of cut by altering the pressure setting. This minimizes the amount of normal tissue that is accidentally removed with normal surgical débriding techniques. The Versajet forces a narrow stream of water across a small gap (8 to 14 mm) at pressure that can reach 15,000 pounds per square inch. This creates a vacuum around the high-pressure water stream (Venturi effect) that sucks in the surrounding tissue and pulverizes it. The softer the tissue,

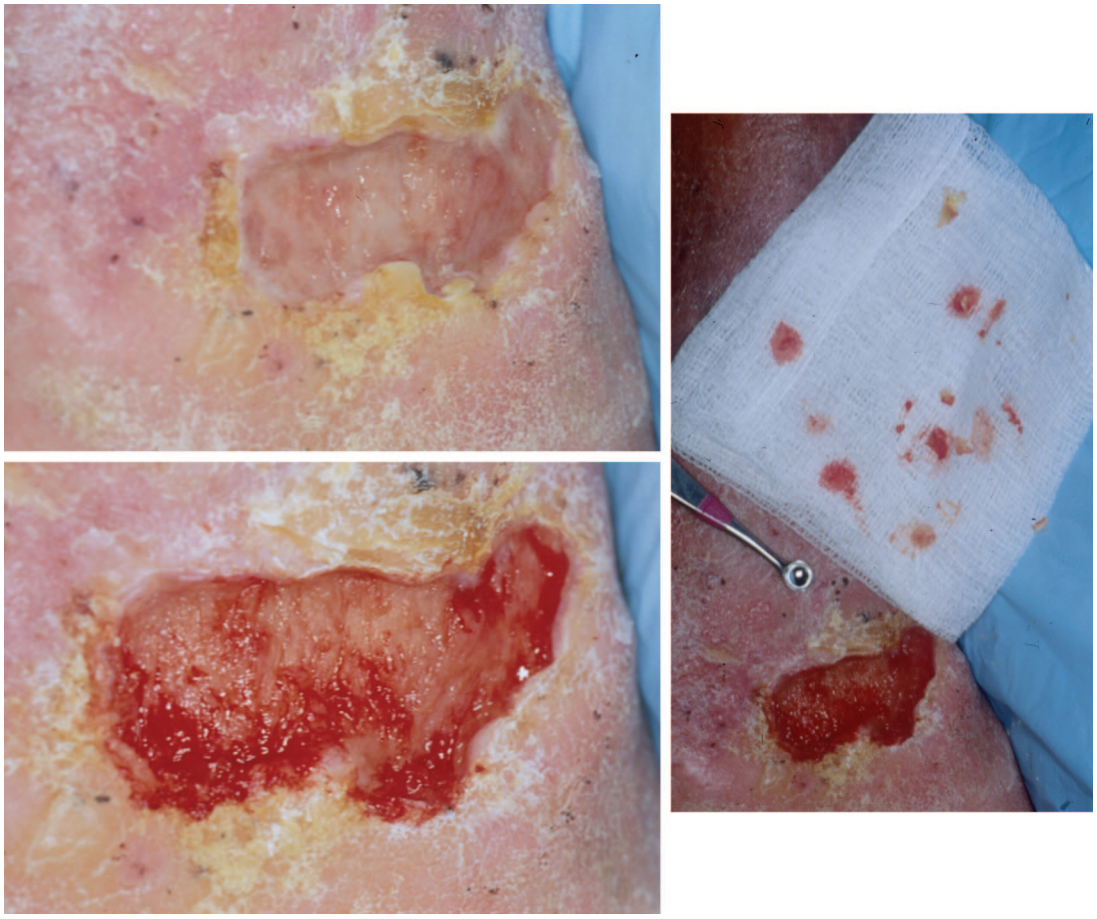

Fig. 11. A curette is very effective in removing chronic unhealthy granulation tissue or proteinaceous coagulum on top of a granulating wound. Placing any wound-healing supplement (growth factor or cultured skin) on a wound requires removal of this coagulum for the supplement to have a chance to be effective.

the lower the pressure settings need to be. It is particularly useful when débriding large areas or when preparing a wound bed for skin grafting (Fig. 13). A pulse lavage system is redundant and therefore not needed when a wound is débrided with the Versajet.

If the wound is going to be closed immediately after débridement, then we use a double instrument set-up in the operating room, consisting of an additional set of instruments, gloves, gowns, drapes, suction, and Bovie, to avoid recontaminating the freshly débrided wound (Fig. 14). After pulse lavage, gloves and gowns are changed, the wound is redraped, and new suction and Bovie are placed on the field. A second table containing new instruments is then used to close the wound. This is to avoid reintroducing bacteria into the débrided and cleansed wound, because cultures of the instrument surfaces used in débriding the wound carry a concentration of bacteria greater than or equal to 10^3 per gram of tissue.[28]

NONSURGICAL TOOLS OF DÉBRIDEMENT

Biological débriding agents, such as maggots, are an effective alternative to surgical débridement in patients who cannot go to the operating room for medical reasons. The larvae of the green blowfly (*Phaenicia sericata*) are sterilized with radiation before they are used, so that they cannot convert from the larvae to the pupae stage.[29–31] They secrete enzymes that dissolve the necrotic tissue and the biofilm that surrounds bacteria. This forms a nutrient-rich liquid that larvae can feed on. Thirty larvae can consume 1 g of tissue per day. They are placed on wounds and covered with a semipermeable dressing. The débridement is painless, but the sensate patient can feel the larvae moving. More importantly, maggots help to sterilize wounds, because they consume all bacteria regardless of their resistance to antibiotics (including methicillin-resistant *Staphylococcus aureus*)

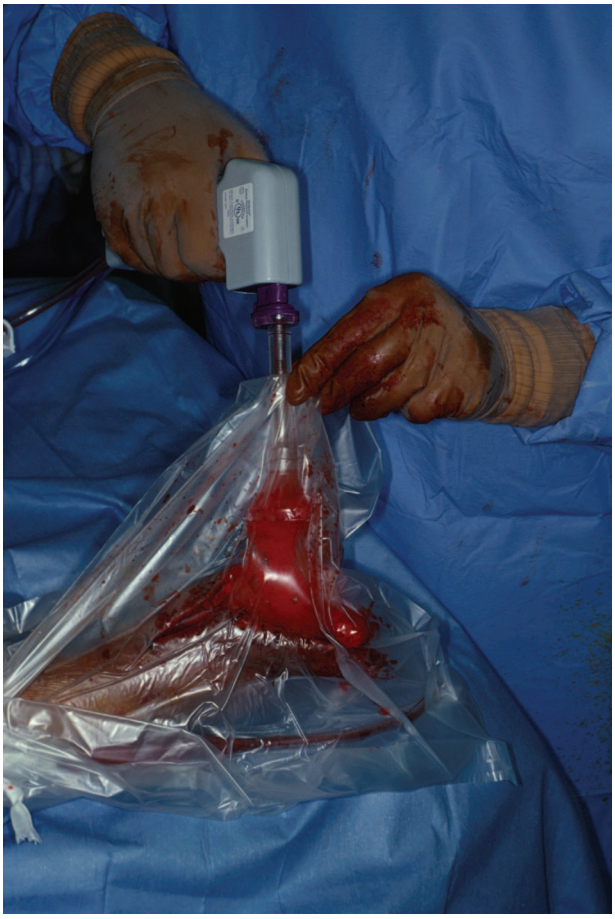

Fig. 12. Placing the débrided extremity in a plastic bowel isolation bag before pulse-evacuating the wound is an effective way to avoid contaminating the rest of the operating room field with the spray from the pulse-evacuation device. A minimum of 3 liters of normal saline without antibiotics should be used on the wound.

and vancomycin-resistant *Enterococcus*). Maggots have to be replaced every 2 to 3 days, and maggot therapy can be administered on an outpatient basis, provided that visiting nurses are familiar with their use.[32] This is a great technique for painlessly removing necrotic tissue and destroying antibiotic-resistant bacteria in patients who cannot undergo surgical débridement for medical reasons. They work well in infected and gangrenous wounds,[33,34] with the best results reported in diabetic wounds.

SURGICAL SKIN DÉBRIDEMENT

Skin débridement consists of removing nonviable, nonbleeding skin. If the injured skin does not blanch, is insensate, and has blistered, it is not likely to be alive. If the macrocirculation is intact, then there is no advantage to waiting and hoping that this skin will suddenly redevelop microcirculation. In this area, there is usually a high concentration of harmful proteases and bacteria that can inhibit wound healing. If not addressed surgically, the slow course of liquefaction necrosis will cause the dead skin to separate from the underlying healthy tissue and may lead to functional loss, bad scarring, deeper tissue damage, and disseminated infection.

Therefore, the approach to nonviable skin should be to remove it as soon as possible.[35] If the border between live and dead tissue is clearly demarcated, then the skin should be excised along that border. If the border is not clearly demarcated, then one should start at the center and slice off thin sections of skin until viable tissue is reached. Viable skin will have punctate bleeding along the dermal edge. Clotted venules reflect a complete interruption in the local microcirculation and mandate further débridement (Fig. 15). Adequately débrided skin should have normal arterial bleeding at the edges and no clotted veins. Deep wound cultures should be obtained of any underlying necrotic tissue.

If the underlying tissue appears viable and not infected, then a biological dressing or negative pressure wound therapy can be used as a temporary dressing. If the tissue is viable but infected, then a topical antibiotic, such as silver sulfadiazine,[7] silver nitrate,[36] or silver-impregnated dressing,[37,38] should be placed on the wound. For *Pseudomonas* infections, 0.25% acetic acid and gentamicin ointment are alternative options. For methicillin-resistant *S. aureus*, mupirocin is a viable topical antibiotic option, although resistance can develop quickly.[39] These options should only be considered temporary dressings between débridements.

DÉBRIDING SUBCUTANEOUS TISSUE

Subcutaneous tissue consists of fat, vessels, and nerves. Because of the decreased concentration of blood vessels in the subcutaneous fat, bleeding at the tissue's edge is not always a reliable indicator of how far to débride. Healthy fat has a shiny yellow color and is soft and resilient. Dead fat has a grey pallor to it and is hard and nonpliable. Fat should be débrided until soft, yellow, normal-looking fat is present. Undermining should be avoided, because it threatens the viability of the overlying skin and the perforating arterial supply may be damaged in the process. It is very important to keep the subcutaneous tissue in a moist environment after débridement, to prevent desiccation.

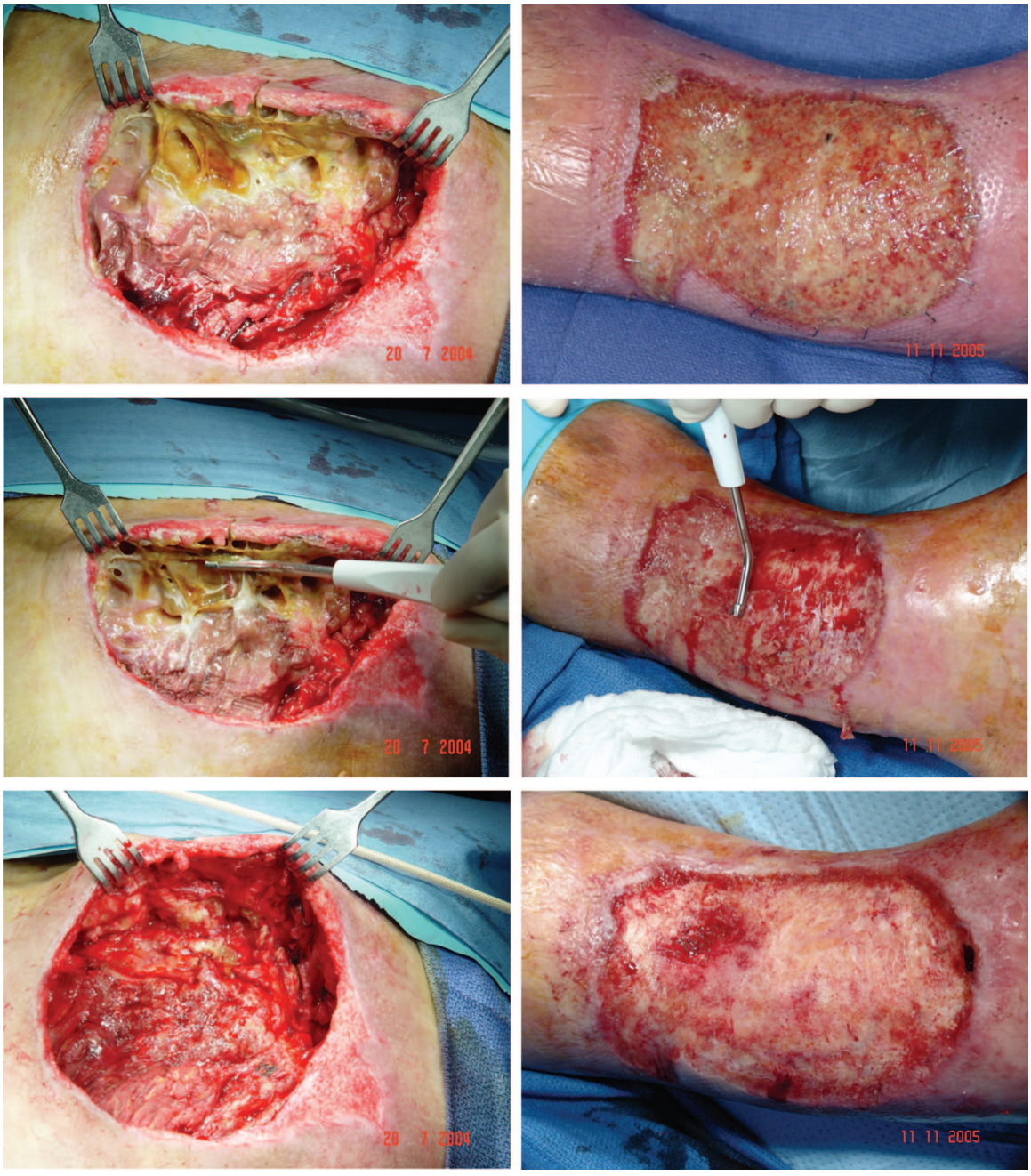

Fig. 13. The Versajet takes off layer after layer of tissue with a high-pressure water jet that creates a local vacuum and sucks the surrounding tissue into the jet. It is an excellent débriding tool (*left*) and is also useful in preparing a wound bed for skin grafting (*right*).

Small blood vessels should be coagulated using bipolar cautery to minimize damage to the surrounding tissue. If the vessels are larger than 2 to 3 mm, they should be ligated with metal clips, which are one of the least reactive foreign bodies. If a suture is to be used, then a small-diameter monofilament suture should be used to minimize the risk of foreign body reaction and possibly facilitating further infection. Silk suture should be avoided, because it acts like a foreign body that initiates a vigorous foreign body reaction. The latter can then become the nidus for bacteria and subsequent infection. Even bacteriostatic polyglycolic woven suture initiates an inflammatory response and has multiple recesses within which bacteria can survive in a semiprotected state.

Nerves, when viable, have a shiny, white, glistening appearance. In subcutaneous tissue, the

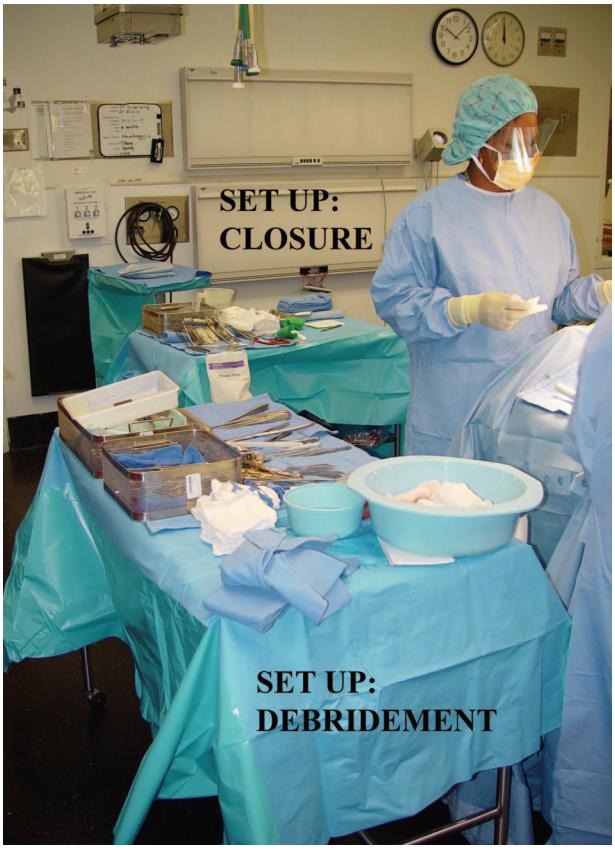

Fig. 14. When débridement and closure are to occur during the same operation, a double instrument set-up, consisting of an additional set of instruments, gloves, gowns, drapes, suction, and Bovie, is used to avoid contaminating the reconstruction of the freshly débrided wound with the dirty débriding tools.

nerves are sensory. Intact exposed sensory nerves in a sensate patient can be very painful. The decision has to be made whether to cut or preserve them. If the nerve is to be preserved, then it has to be kept moist until it can be covered with adequate tissue. Usually a skin graft does not provide sufficient padding to prevent pain on contact. Consideration should be given to burying the nerve underneath other tissue or a flap. If the nerve is to be sacrificed, then the nerve should be placed on traction, cut proximally, and allowed to retract within normal tissue. Alternatively, to help avoid neuroma formation, the end can be buried in underlying muscle or bone or the epineurium can be sewn over the nerve fascicles using 8-0 or 9-0 nylon.

DÉBRIDING FASCIA, TENDON, AND MUSCLE

Healthy fascia has a white, glistening, hard appearance and should be preserved if it looks viable. When fascia is dead, it appears dull, soft, and stringy and is in the process of liquefying; it should all be débrided. Since neurovascular bundles can be close to overlying fascia, débridement should proceed with caution. The healthy fascia must be kept moist after débridement to avoid desiccation.

The underlying muscle must be examined as well. Healthy muscle has a bright red, shiny, and resilient appearance and contracts when grasped with forceps or touched with cautery. The caveat is that in neuropathic patients, the muscle may have a pale, perhaps yellowish color and may appear nonviable. Viable muscle in these patients will have some tone and will bleed when cut. Frankly dead muscle will be swollen, dull, and grainy when palpated and falls apart when pinched. If viability of the muscle is questionable, it is best to err on the side of caution and remove only what is not bleeding. In general, only muscle that is clearly dead should be removed to avoid further unnecessary dissection that might compromise blood flow to the surrounding tissues (i.e., overlying skin).

Tendon débridement is complicated, because sacrifice of this structure may lead to loss of function. All attempts should be made to preserve the viable paratenon, an encapsulating shiny coating that provides nutrition and prevents desiccation of the tendon. If the paratenon is not preserved, the tendon must be kept moist after débridement. Tendons should be covered with viable tissue as soon as the wound is stable. Otherwise, the tendon will desiccate and necrose, which can result in infection and loss of function. Infected tendon looks dull, soft, and grainy, with parts separating and/or liquefying (Fig. 16). Smaller tendons with infection should be removed en bloc. It is important to *make proximal and distal incisions to the exposed tendon* to ensure that any hidden necrotic tendon and/or infection is uncovered.

When the tendon is large (e.g., Achilles tendon or anterior tibial tendon), only that portion of the tendon that is necrotic or infected should be débrided. The hard, shiny tendon underneath should be left intact. Great care should be taken to keep the remaining tendon moist. The Achilles tendon deserves special mention because it is so large and receives excellent blood supply from both the posterior tibial and peroneal arteries. If it is exposed and healthy, there are many reconstructive option that may be used, including skin grafts and local, pedicled, or free flaps.[40] If part of the tendon is necrotic, it should be débrided to hard, shiny tendon. Serial débridement may be

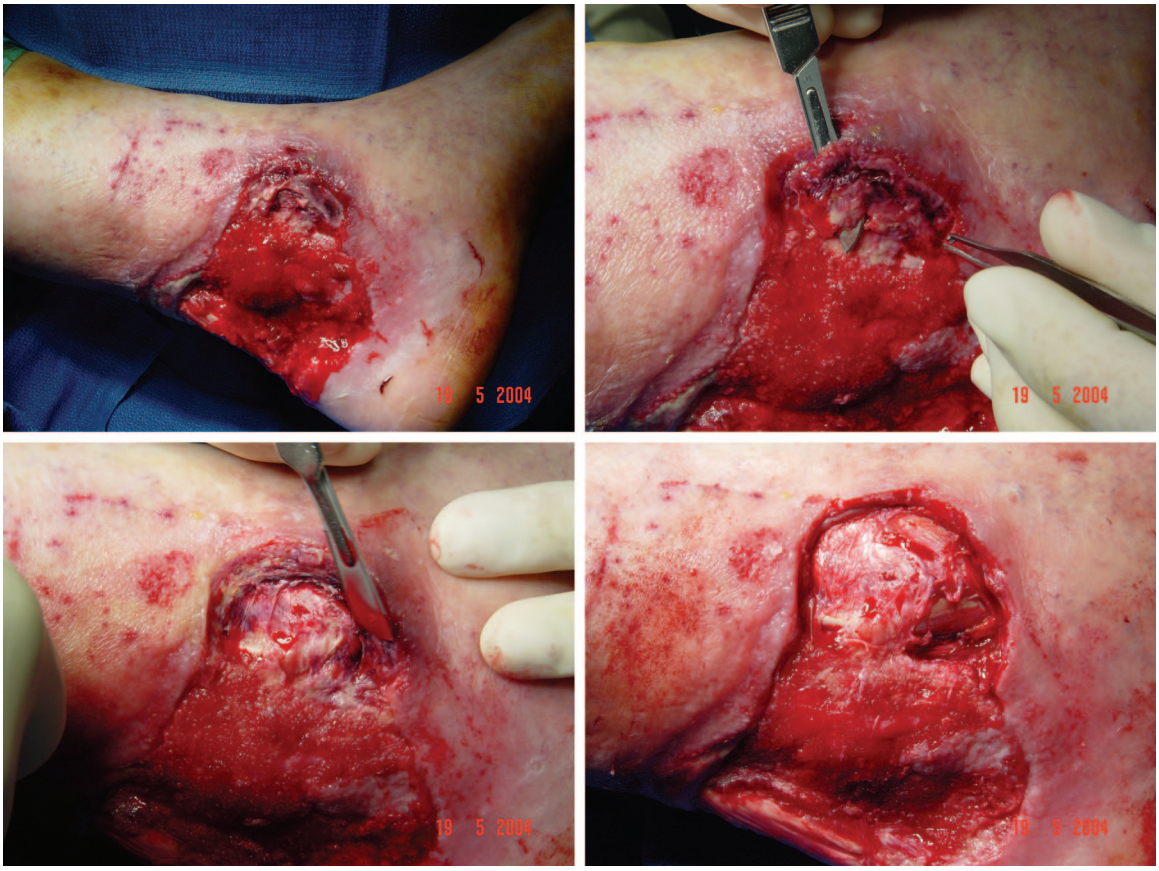

Fig. 15. (*Above, left*) Preoperative view. (*Above, right*, and *below, left*)The skin and subcutaneous tissue are débrided until normal-looking tissue and bleeding are obtained. The presence of clotted veins in the soft tissue means that the local circulation is interrupted and that further débridement is needed to reach to normal-looking tissue (*below, right*).

necessary until healthy granulating tendon is achieved. Negative pressure wound therapy, growth factors, bioengineered tissues, and/or hyperbaric oxygen can be used to accelerate the process (Fig. 17).

DÉBRIDING BONE

Nonbleeding bone is characteristic of necrotic or dead bone. It may also be soft and discolored. All soft, nonbleeding bone should be removed. Bone should be débrided to punctate bleeding on the cortex (paprika sign) and normal-looking marrow in cancellous bone. Useful tools to accomplish this include rongeurs, curettes, and rasps. Power tools, such as the sagittal saw and the cutting burr, may be required for larger bones or those that require extensive débridement and/or amputation. Care should be taken not to shatter contiguous viable bone. In this regard, power tools are safer to use than rongeurs or chisels. The best way to débride infected smaller bones (phalanges, metacarpals, or metatarsals) is to serially saw slices of bone (Fig. 18) until healthy bone is reached. For abnormal cortex of larger bones (e.g., tibia, fibula, radius, or ulna), a cutting burr that shaves thin layer after thin layer of the questionable bone until only healthy bleeding bone remains is more useful (Fig. 19). Copious irrigation should be used to ensure that the heat generated by the burr does not damage the healthy bone.

The removal of all osteomyelitic bone always takes precedence over the preservation of normal bony architecture. Modern orthopedic techniques, including bone grafting, distraction, and osteoinductive growth materials, can be used to repair most bone defects. Use of the Ilizarov technique allows the placement of fine wire external fixation for bone stabilization without internal hardware. The frames limit access to soft tissues, so close coordination between the plastic surgeon and the orthopedic or podiatric surgeon is essential during its placement to allow optimal soft-tissue exposure without sacrificing bone stability. If more exposure is needed, a portion of the frame can be removed during the soft-tissue repair.

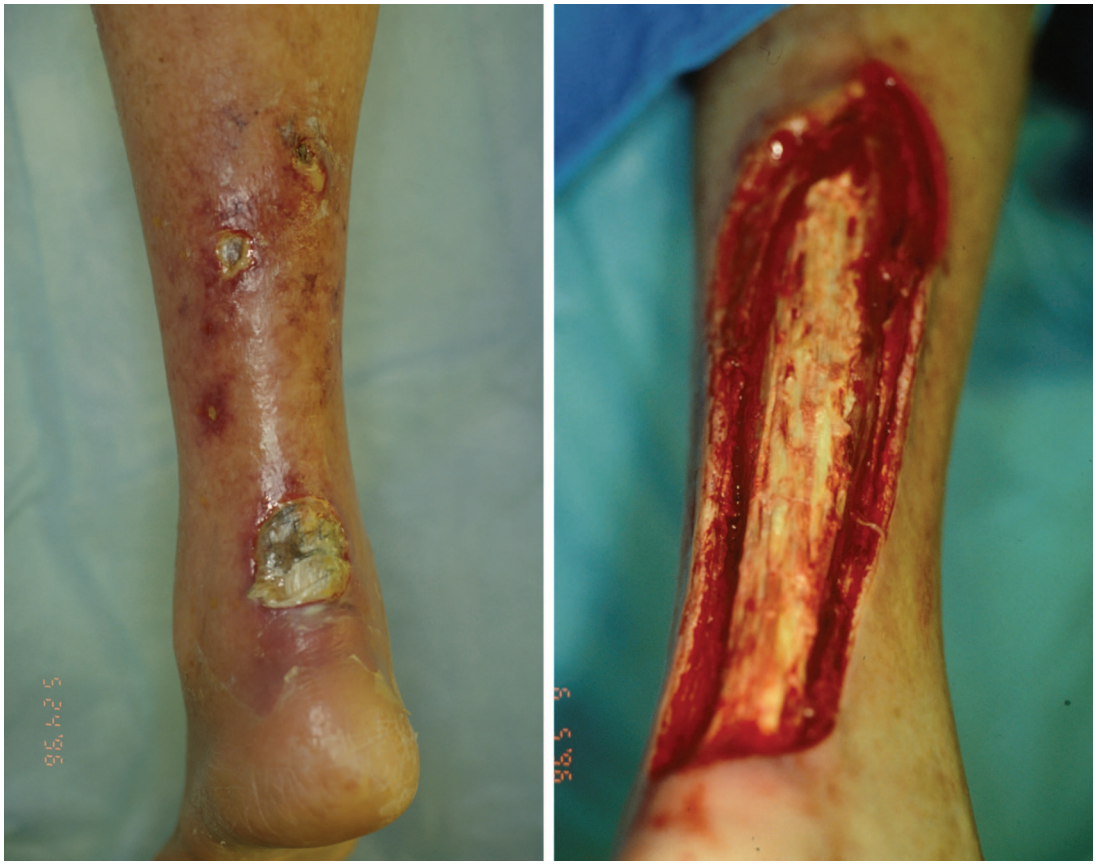

Fig. 16. (*Left*) An infected Achilles tendon in the stages of liquefaction. The area proximal and distal to the exposed tendon was explored to make sure that all necrotic tendon was removed. (*Right*) After débridement to hard shiny tendon, there was sufficient tendon left behind to preserve function. This wound was later covered with a free flap.

It is important to obtain cultures of both the débrided osteomyelitic bone and the normal bone proximal to the area of débridement. A 6-week course of antibiotic therapy for the infected osteomyelitis is no longer the accepted course of therapy if the involved infected bone has been surgically removed.[41] When only healthy bone remains at the base of the wound, a 1-week course of appropriate antibiotics usually suffices. The exception to a 1-week course of antibiotics after closure is when the surgeon suspects that the bone left behind may still harbor osteomyelitis (e.g., calcaneus or tibia). In that case, a longer course of antibiotic therapy is needed. The appropriate antibiotic course is best determined and monitored by an infectious disease physician for treatment as well as for untoward side effects.

SPREAD OF INFECTION ALONG TISSUE PLANES

With infection penetrates to deeper levels, it is important to rule out the spread of infection and/or necrosis spread along anatomic planes. During deep tissue débridement it is crucial to understand the anatomy to aid in the exploration of all possible areas that can harbor infection. This is best illustrated in necrotic and purulent ulcers overlying tendon or muscle, where infection can spread along tendon sheaths and/or fascial planes. For example, the flexor tendon sheaths, peroneal tendon sheaths, and extensor tendon sheaths are possible avenues of spread in any necrotic plantar foot ulcer. Evaluation of infection within those possible routes includes feeling for bogginess of the overlying tissue as well as needle aspiration or direct exploration of the actual tendon sheath. A small incision in the skin directly over the suspect tendon sheath, followed by gentle spreading with a straight clamp, will reveal whether purulence is present. It is also useful to milk the tissue overlying the questionable tendon sheath toward the ulcer site and look for purulence emanating at the ulcer site. Great care should be taken to ensure that the incision and dissection have gone far enough proximally. The proximal and or distal ex-

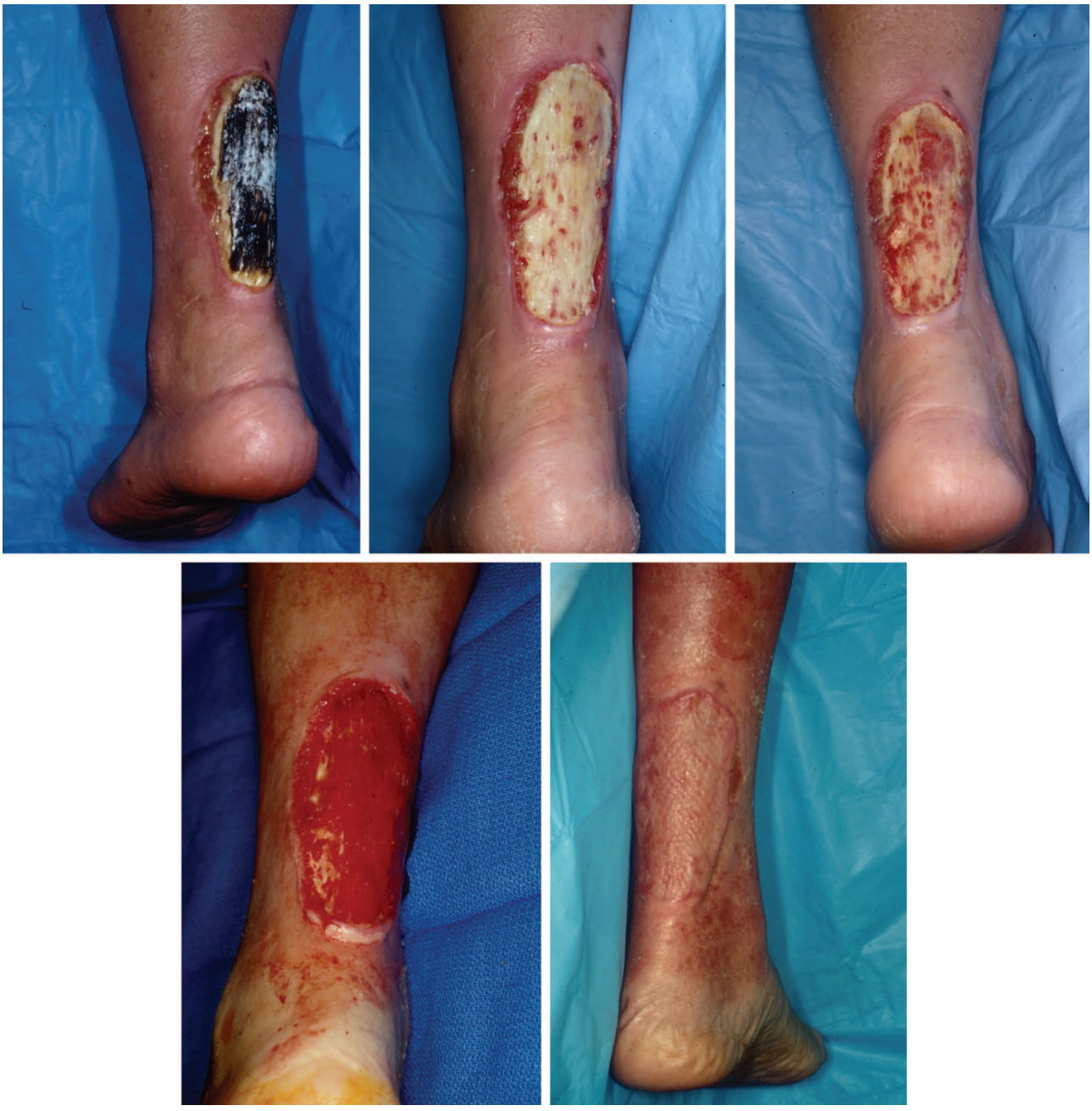

Fig. 17. (*Above, left*) A patient presented with a gangrenous Achilles tendon. (*Above, center*) The necrotic tendon was sharply débrided to shiny underlying tendon. Hyperbaric oxygen and topical growth factor therapies were started, and the tendon began to granulate (*above, center*, 1 week; *above, right*, 2 weeks; *below, left*, 3 weeks). The Achilles tendon was then successfully skin grafted and healed completely after 4 weeks (*below, right*).

ploration should stop only when the surrounding tissue has a normal appearance. This may require filleting the foot, ankle, and leg all the way up to the popliteal fossa, or the hand, wrist, and arm all the way to the antecubital fossa. With extensive infection, repeated débridement every 12 to 48 hours should be performed until the wound is free of infection. This aggressive approach is often the only chance to save an extensively infected limb.

When the blood supply is adequate, progressive tissue necrosis after débridement usually represents lingering uncontrolled infection and is an indication for further débridement. It is also important not to condemn a limb to amputation too quickly when the amount of infection present requires extensive débridement. With necrotizing fasciitis, the tissue damage is often only limited to the fascial tissue and overlying subcutaneous tis-

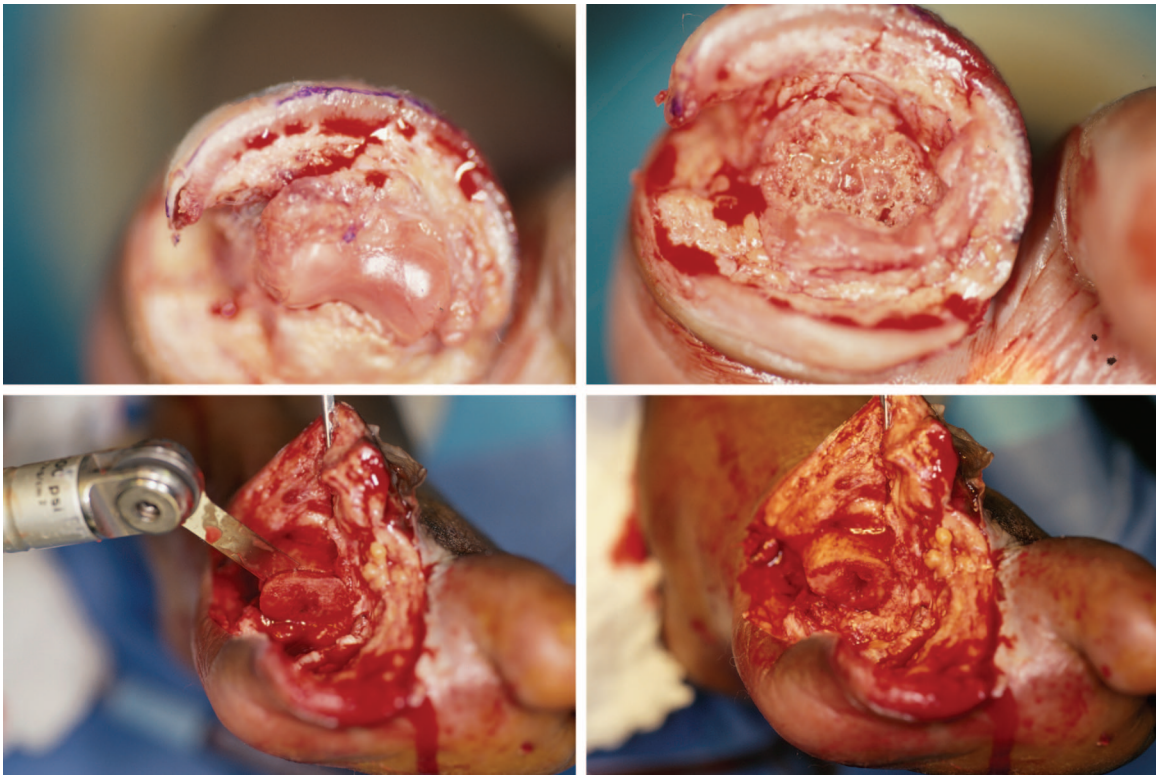

Fig. 18. Infected bone should be débrided back to hard, bleeding cortical and cancellous bone using a cutting burr or rasp. Here, the distal portion of the proximal phalanx has a dull almost purple color (*above, left*). The head was rongeured back and the bone was nonviable (*above, right*). To avoid shattering the proximal bone, a sagittal saw was used (*below, left*) to serially slice the bone until healthy bleeding cortical and cancellous bone was reached (*below, right*).

sue and skin. Serial débridement may not require the sacrifice of the underlying tendons and muscle. In that instance, the wound can eventually be closed with a simple skin graft. Alternatively, if the débridement process leaves the foot and leg with what appears to be a formidable reconstructive challenge, modern limited amputation and reconstructive techniques can usually salvage a functional limb.

APPROACH TO THE ACUTE WOUND

The acute wound has not yet gone through the normal healing phases. The patient should receive a tetanus booster if the tetanus status is unknown or not up to date (within 5 years). The wound should be cleansed of contaminants and dead tissue as soon as possible. This may be done initially in the emergency room or in an office with proper equipment. If more extensive débridement is anticipated, the patient will need to be débrided in the operating room. When there is a delay in getting to the operating room in an urgent situation, a peripheral nerve block can facilitate the emergency room or office débridement. Cultures of the actual débrided tissue and loose bone fragments should be analyzed, as these have been shown to best correlate with future cultures of osteomyelitis.[42] The wound is best cleansed with pulsed lavage using several liters of saline. Adding antibiotics to the lavage solution does not contribute to wound cleansing.[43]

If there is any question of a compartment syndrome, the pressures should be checked and the appropriate compartment(s) should be released.

Once the cultures have been sent, the patient should be started on broad-spectrum antibiotics[44] for better coverage of anaerobic and Gram-negative bacteria. Antibiotics can then be adjusted for more specific coverage when the initial deep wound culture results with sensitivities are interpreted.

In the operating room, the goal of the initial débridement is to remove all obvious dead skin, subcutaneous tissue, fascia, muscle, and bone while leaving behind all potentially viable tissue. If the skin and subcutaneous tissue are avulsed,

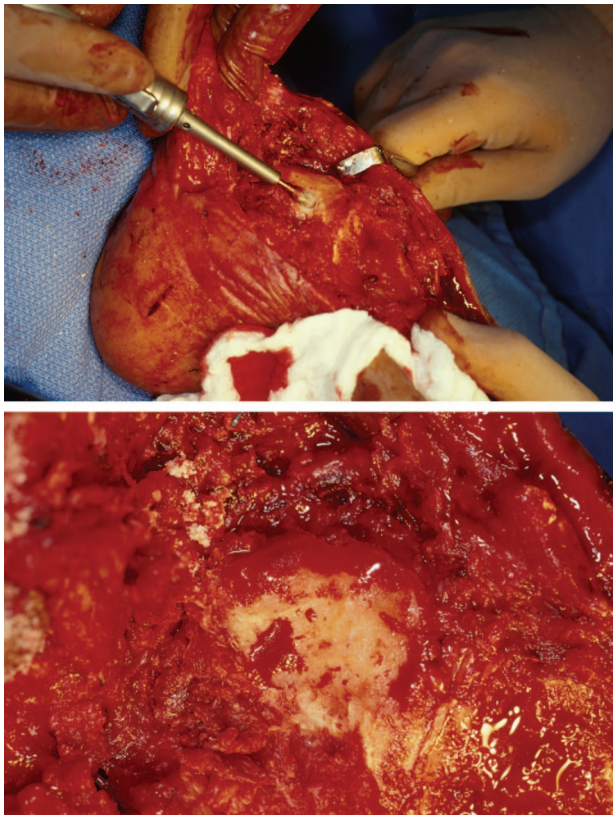

Fig. 19. For larger bone, a cutting burr is used to remove thin layer after thin layer of bone (*above*). It is important to irrigate the bone during the process to avoid damaging it with the heat from the burr. The presence of punctate bleeding at the surface of cortical bone indicates viable bone (paprika sign) (*below*).

there is an overwhelming chance that much of it will die because of disruption in the blood supply. Therefore, avulsed tissue should be trimmed until actual bleeding at the skin edge is seen. Deep cultures of the wound should also be obtained. The anatomic damage should be fully evaluated, including avulsed nerves and/or tendons. Cut nerves should be tagged with a fine monofilamentous suture, so that they do not become lost in the subsequent soft-tissue swelling. The wound should then be cleansed with pulse lavage to remove all foreign debris and dressed in a continuously moist, nonirritating bandage that keeps exposed tendons, fascia, and bone from desiccating. An alternative dressing is the negative pressure wound therapy device, which can be applied directly on the wound to reduce the bacterial load and keep the edema to a minimum. Recent reviews show that this an extremely effective dressing in the setting of acute trauma and partial amputation wounds.[25,45,46]

Serial débridement every 24 to 48 hours is recommended until the wound has only viable tissue and is soft and without erythema. This type of wound is then ready for closure. Before the advent of the negative pressure wound therapy device, it was important to get the wound ready for reconstruction within 7 days from the date of injury, to minimize complications.[47] Because the negative pressure wound therapy device decreases the bacterial count in the wound as well as the edema, it has proven to be very effective in extending the 1-week "golden period" within which the wound should be covered. The negative pressure wound therapy device should not, however, remove the surgeon's sense of urgency in achieving wound closure.

APPROACH TO THE INFECTED WOUND

In the infected wound, it is important to know the source and extent of the infection. The edge of the erythema around the wound should be delineated and timed and dated. This is then used as a reference point for effectiveness of the chosen antibiotics and/or débridement (Fig. 3). Obtaining a radiograph of the affected area lets the physician know whether the bone is involved and whether gas is present in the soft tissue (Fig. 20). If gas is seen within the tissue planes on the radiograph, then gas gangrene is present and the wound becomes a surgical emergency. This gas is usually a byproduct of anaerobic bacteria (usually *Clostridia perfringens*); it tends to be foul smelling and to travel along the fascial planes. Compartment pressures in the affected area should be checked, because high pressures in the diabetic foot with gas gangrene are frequently missed.[48] If there is a question of a deep abscess, ultrasound imaging or computed tomography scanning can be very useful.

Before emergency débridement is performed, one has to assess whether there is sufficient blood supply to eradicate the infection and heal the wound. Insufficient blood flow inhibits the body from delivering the necessary white blood cells, nutrients, oxygen, and antibiotics to the wound site. Palpable or Dopplerable triphasic or biphasic pulses usually signify sufficient inflow. In the case of questionable inflow, noninvasive vascular studies should be performed after the débridement. If the flow is deemed insufficient, the affected extremity should be revascularized as soon as possible. Unless there is gas gangrene or a rapidly ascending infection, débridement should be limited to removing only the frankly necrotic tissue until the limb has been adequately revascularized.

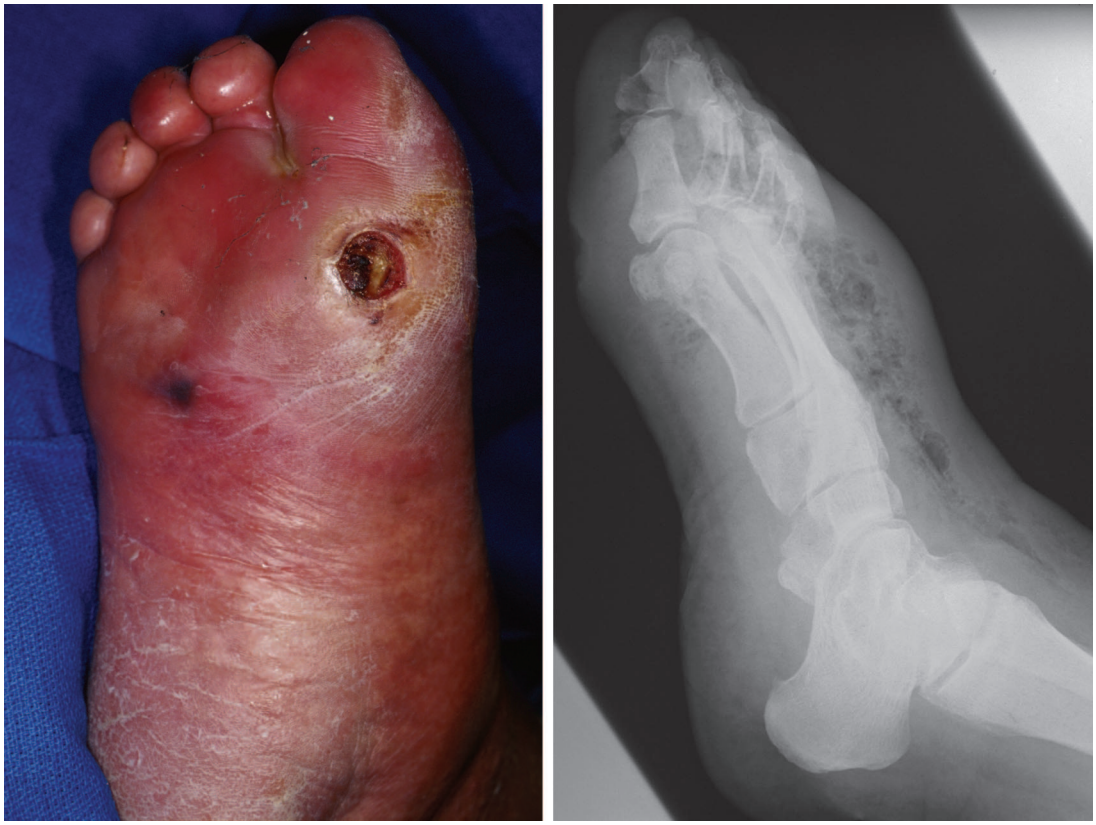

Fig. 20. (*Left*) A diabetic patient with a plantar ulcer rapidly developed a massively swollen and erythematous foot that had crepitus when examined. (*Right*) The radiograph revealed gas both on the plantar and dorsum of the foot. The patient was taken to the operating room immediately for radical débridement. It is important to remember that while the tissue usually involved is at and above the fascial layer, there may be elevated compartment pressure underneath.

If the wound is acutely infected with purulence, with odor emanating from it or with proximally ascending erythema, it needs to be débrided immediately and very aggressively to prevent limb loss or death. The involved compartments of the extremity should be released if there is any question that the compartment pressures are abnormal. Wounds with foul-smelling odors should be cleaned so that at the end of the débridement, any residual odor in the wound is gone (Fig. 21). If the foul odor is still present, then the débridement is incomplete and there is more necrotic or infected tissue present that needs to excised. It is important to remember that just because an extremity presents with gas gangrene, it should *not* be summarily amputated, because aggressive repetitive débridement and hyperbaric oxygen can often salvage enough of the limb to preserve a functional extremity. Hyperbaric oxygen has been shown to be particularly helpful in the control of anaerobic infections.[49]

Aerobic and anaerobic cultures of the wound are obtained during the débridement by taking pieces of deep infected tissue and purulence. A swab or superficial tissue culture is of limited use, because it usually reflects surface flora rather than the actual underlying bacteria responsible for the infection. One should then débride the wound as specified above and start broad-spectrum antibiotics after the deep tissue cultures have been obtained. The antibiotic spectrum can be narrowed as soon as the culture sensitivities become available.

Persisting signs of infection may warrant a return to the operating room immediately and every 12 to 24 hours for redébridement due to suspicion of undrained purulence or necrotic tissue. Hydrogen peroxide, 1% Dakin's solution, povidone iodine, or chlorhexidine are bacteriocidal and help sterilize the wound. However, these agents also destroy normal tissue and should therefore only be used when there is residual undébrided gangrene or necrotic tissue left in the wound. If only viable tissue lies at the base of the wound, topical therapy should be gentle enough to promote, rather than hinder, healing. Appropriate topical

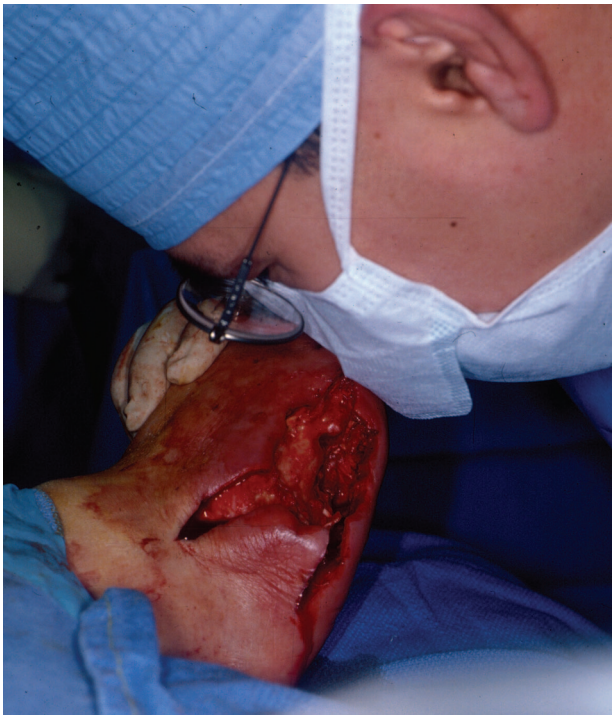

Fig. 21. When débriding a foul-smelling wound, one should continue until the entire odor is gone from the wound. Persistent odor signifies residual undébrided infection in the wound.

antibiotics, such as silver sulfadiazine, may be useful because they can help control the local infection while minimizing damage to the underlying normal tissue. The negative pressure wound therapy device is an excellent topical dressing, provided that the wound is free of grossly contaminated tissue. Placing the negative pressure wound therapy device on an infected wound can lead to toxic shock syndrome.[50] If there are any exposed neurovascular structures, protective silicone sheeting should be placed between the base of the wound and the negative pressure wound therapy sponge.

APPROACH TO THE CHRONIC WOUND

Chronic wounds are superficially colonized with bacteria and may harbor a deeper infection. The difficulty in treating the chronic wound lies in accurately establishing the etiology, as débridement may not necessarily be the first step in treatment. An example is vasculitic ulcers, for which the underlying illness first needs be addressed medically. A biopsy at the wound periphery that includes normal tissue may be required to make the diagnosis. Fifty percent of vasculitis patients also suffer from a coagulopathy that may be a contributing factor to their ulceration.[51] If the wound is due to venous stasis disease, the venous system should be assessed for venous incompetence or thrombosis by venous Doppler studies. These patients may benefit from superficial venous stripping, ligation of perforators, or valve transposition. Venous stasis patients who have a history of thrombosis should likewise be evaluated for coagulopathy that may require medical therapy. If the wound is due to arterial insufficiency, the affected limb should first be revascularized. Neoplastic lesions should be suspected in chronic wounds that do not heal and continue to ulcerate. Performing a biopsy or sending the excised ulcer for pathologic analysis to obtain a definitive diagnosis best accomplishes this. Radiation wounds have been shown to heal more effectively with adjuvant hyperbaric oxygen therapy.[52] Dermatologic manifestations of hematological abnormalities (e.g., clotting abnormalities, sickle cell, thrombocytosis, cryoglobulinemia, and so on) should be medically managed until the patient's hematological condition has been optimized. If the etiology is unclear or pyoderma gangrenosum is suspected, the wound should be biopsied and may necessitate referral to a dermatologist for treatment.

Hyperglycemia, especially blood glucose levels above 200 g/dl, causes dysfunction of polymorpheonucleocytes which then hinders their ability to guide the wound-healing process.[53–55] Diabetic wound healing proceeds far more effectively when tight glycemic control is maintained. The hemoglobin A1C level is a good indicator of blood glucose controls over the previous 3 months. Any discrepancies or problems maintaining normal blood glucose levels should be referred to an endocrinologist. Smoking has been shown to have deleterious effects on wound healing, because one cigarette decreases local blood supply by up to 30 percent for 2 to 4 hours after each cigarette.[56–59] Insisting that the patient stop smoking during the wound-healing period may play a crucial role in the outcome (Fig. 22).

After the cause of the wound has been determined and treated, débridement of the ulcer should be the next step. This is done to recreate an acute wound that can now progress through the normal stages of healing. This is usually achieved with serial débridements until bleeding, soft, normal-colored tissue is reached. Normal tissue may be difficult to find in chronic venous stasis disease or in radiation wounds. The amount of resection necessary to get there may require removal of so much tissue that reconstruction may not be possible. In these instances,

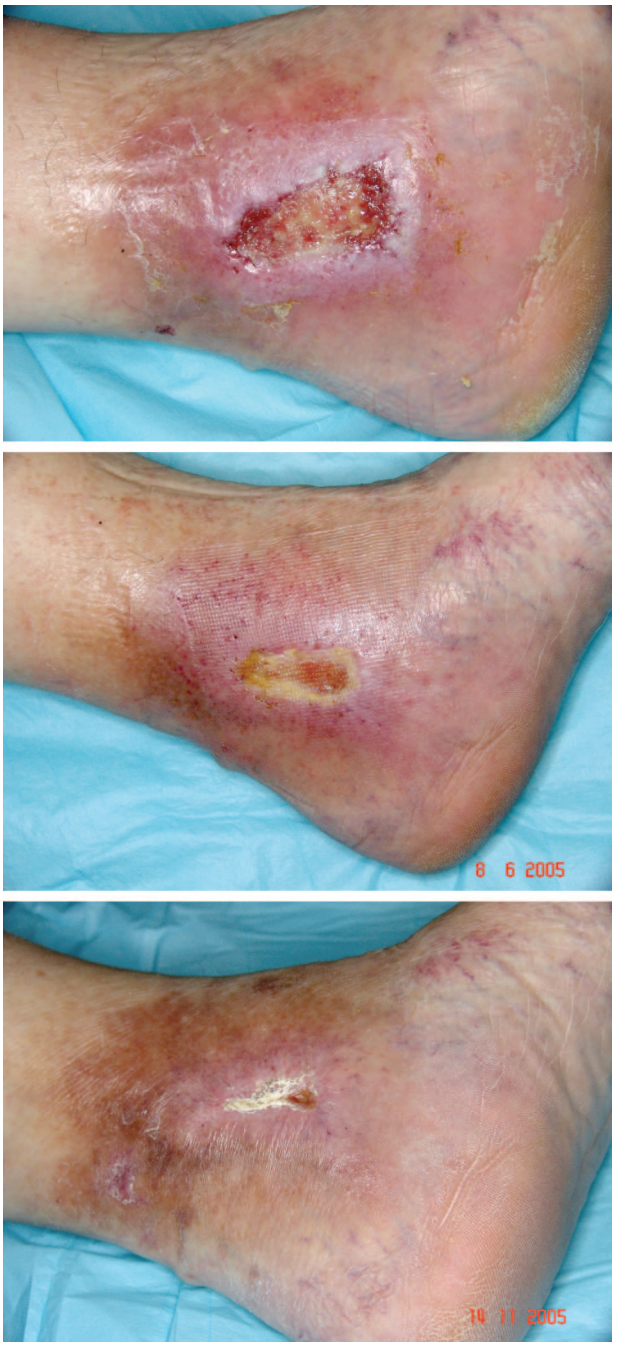

Fig. 22. (*Above*) A diabetic patient with vasculitis and a long-term, nonhealing wound. (*Center*) Despite aggressive wound therapy for more than 1 year, the characteristics of the wound did not change. (*Below*) When the patient stopped smoking, the wound made an immediate turnaround and started healing.

rather than débriding to normal tissue, it is preferable to débride to good bleeding scar tissue. This scar tissue, although indurated and stiff, can granulate in and eventually be covered with a skin graft or a flap.

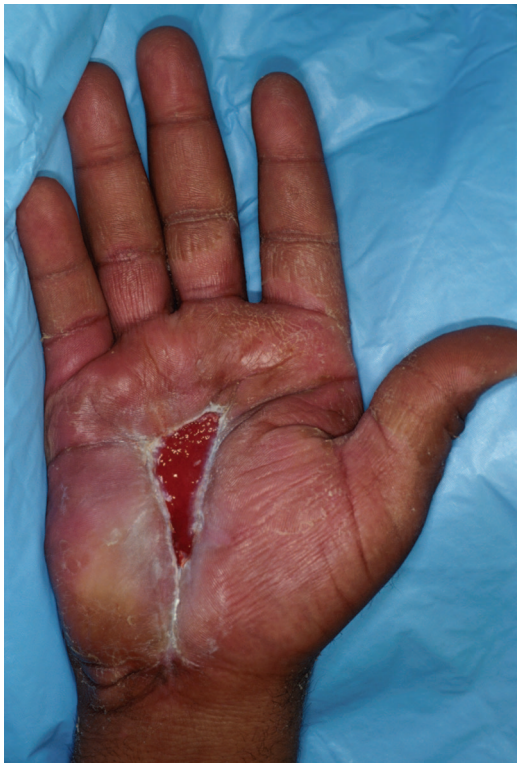

Fig. 23. This wound has all the physical signs of healthy healing. The color of the granulation is bright red, and the granulation buds are very small. There is epithelialization at the border, and there is wrinkled skin around the wound.

MODERN WOUND-HEALING STRATEGIES TO STIMULATE HEALING

Once débridement has achieved a clean, well-vascularized wound, the focus should then be on providing the optimal environment for healing: moist, clean, and vascularized, to enable the use of growth factors and inhibiting metalloproteases. Moist healing[60] has been shown to be far more rapid than healing under an eschar.[61] In this environment, the wound base can support and promote successful collagen deposition, angiogenesis, epithelialization, and wound contracture. The result should be the formation of healthy red granulation tissue, with neoepithelialization at the borders (Fig. 23).

To assess whether the current conditions for healing are adequate, it is necessary to measure to size of the wound on a weekly basis. A reduction in the area of the wound of 15 percent or more per week represents normal healing.[62–66] If the healing is occurring at a slower rate, then the cause of the wound, the blood supply, and the medical condition of the patient should be reevaluated. The wound strategy should then be re-evaluated and adjunctive wound-healing modalities should be

considered at every visit. It is critical to prescribe the use of adjunctive products based on evidence-based data to ensure the most reliable response.[67]

Wound Characteristics and Dressings

There is no single dressing suitable for all types of wounds, and often a number of dressing types will be needed throughout the healing process. Ideally, a dressing should perform as many of the functions listed below as possible:

- Maintain high humidity at the wound/dressing interface
- Remove excess exudate.
- Promote gaseous exchange
- Provide thermal insulation
- Be impermeable to bacteria
- Keep the wound free of particles and toxic wound contaminants
- Be removable without causing trauma

After accounting for systemic patient factors, the simplest way to choose the most appropriate dressing is to observe the wound bed characteristics. (1) If the wound is dry or desiccated, add moisture. (2) If the wound is draining, absorb the exudate. (3) If the wound is necrotic, débride it. (4) If the wound is infected, treat it with antimicrobial therapy. As the characteristics of the wound bed change, the dressing must also change. A caveat with topical wound dressings and adjuvants is to be cognizant to sensitivities or contact dermatitis that may render the treatments more detrimental than beneficial.

Silver-containing dressings are the newest evolution in advanced wound care, and are found in conjunction with many products.[37,38] Silver ions kill a broad spectrum of bacteria, including highly resistant bacteria such as methicillin-resistant *S. aureus*, vancomycin-resistant *Enterococcus*, and *Pseudomonas aeruginosa*. Resistance to silver has not been shown, and it is nontoxic to human cells. In addition, it is an ideal antimicrobial barrier for preventing critical colonization of the wound bed. Although individual silver dressings are expensive (approximately $35 per 4 × 4 sheet), the sustained-release mechanism allows them to be more cost effective than daily dressing changes. Since they have been shown to affect keratinocytes in culture, silver-containing dressings should be limited to infected wounds (see "Effect of Different Wound Dressings on Cell Viability and Proliferation," by Paddle-Ledinek et al., in this issue).

Table 1 lists the dressing types, the principal function they perform, and a sample of many commercially available dressings that fit a given category. The manufacturer and/or U.S. distributor is listed for convenience. The list is by no means exhaustive or meant to disparage dressings not listed. It is meant to give the clinician an idea of where frequently used dressings that are currently available fit in the treatment algorithm. Use of the vacuum-assisted closure device as a dressing is addressed below and should be considered a viable option in granulating and exudative wounds.

WOUND TYPES

Unbroken Skin

Unbroken skin is characterized by intact skin that remains reddened for more than 1 hour after relief of pressure. This is thought to be secondary to pressure ischemia resulting from constant pressure sufficient to impair local blood flow to soft tissue for an extended period. Preventative measures are aimed at providing pressure relief by turning patients regularly, off-loading bony prominences, and using alternatives to the standard hospital foam mattress, such as low-air-loss mattresses or foam overlays.[68]

Treatment options are similarly aimed at pressure relief and increasing local circulation. Pressure ulcers were found to be best healed in patients using air fluid supports.[69] Further, a topical ointment composed of castor oil, trypsin, and balsam peru (Xenaderm; Healthpoint, Fort Worth, Texas) has shown efficacy in both treatment and prevention of these stage 1 pressure ulcers secondary to vasodilation.[70]

Epithelializing Wounds

Epithelializing wounds are characterized by a pink neoepithelium that usually creeps in from the edges (Fig. 24). These wounds are usually considered to be in the proliferative phase of healing, and thus systemic factors, as well as local mediators, are working together to heal the wound. Providing an optimal milieu enables these wounds to continue through proliferation and then progress toward a healed wound. Studies have shown that a moist wound bed allows for unimpeded epithelial cell migration, leading to faster closure rates.[71–73] Occlusive dressings preserve the voltage gradient across the wound, which is felt to play a role in the rate of epithelial migration.[74,75] Dry wounds loose the above voltage gradient.

There are a multitude of adjuvants designed for moisturizing the epithelializing wound bed. Hydrogels are cross-linked polymer gels or sheets and are available with adhesive borders as well as

Table 1. Dressing Class, Principle Properties, Sample of Commercially Available Dressing Subtypes

Type of Dressing	Characteristics	Commercially Available Products
Hydrogels	• Cross-linked polymer gels or sheets • Available with adhesive borders as well as silver ion-impregnated formulations • Generally waterproof, which may prevent bacterial and environmental contamination; their high water content inhibits absorption of exudates, but they are also hydrophilic in nature, which may allow evaporation of exudates • Change daily to every 7 days	• AquaGauze (DeRoyal, Powell, Tenn.) • Aquasite (Dumex Medical, Toronto, Canada) • CarraDres (Carrington Laboratories, Irvin, Texas) • Curasol (Healthpoint, Fort Worth, Texas) • Intrasite (Smith & Nephew, Largo, Fla.) • Skintegrity (Medline, Mundelein, Ill.)
Film/transparent	• Adhesive, semipermeable, polyurethane membrane dressings that vary in thickness and size • Waterproof and impermeable to bacteria and contaminants • Allow for observation of the wound bed • Should not be used on fragile skin or with wounds that have moderate to heavy exudates	• Bioclusive Transparent (Johnson & Johnson Wound Management, Somerville, N.J.) • Mefilm (Molnlycke, Newtown, Pa.) • OpSite (Smith & Nephew) • Tegaderm (3M Healthcare, St. Paul, Minn.)
Foams	• Hydrophilic polyurethane/polymer or gel-coated dressings • Support autolytic débridement • Minimal to moderate absorption capability • Maintain a moist wound environment • Nonadherent • Not to be used over dry eschars • Do not prevent periwound maceration in heavily exudating wound • Come as pads, sheets, and cavity dressings • Change daily to every 7 days	• Allevyn (Smith & Nephew) • Curafoam (Tyco Healthcare/Kendall, Mansfield, Mass.) • Lyofoam (Convatec, Skillman, N.J.) • Mepilex Border (Molnlycke, Newtown, Pa.) • Optifoam (Medline) • Polymem (Ferris Manufacturing Corp., Burr Ridge, Ill.) • Tielle (Johnson & Johnson Wound Management)
Alginates	• Made of brown seaweed • Absorbs up to 20 times its weight • Wicks fluid away from wound bed • For use in moderate to heavily exudating wounds • Subset of hydrofiber dressings absorbs 30% more exudates (Aquacel), although not as effective as a wick • Ideal as a dead space filler	• Algicell (Dumex Medical) • Algisite (Smith & Nephew) • Aquacel (Convatec) • Carrasorb (Carrington Laboratories) • Curasorb (Tyco Healthcare/Kendall) • Kalginate (DeRoyal) • Kaltostat (Convatec) • Maxorb (Medline) • SeaSorb (Coloplast, Marietta, Ga.) • Silvercel (Johnson & Johnson Wound Management) • Sorbsan (Bertek Pharmaceuticals, Research Triangle Park, N.C.)
Hydrocolloids	• Occlusive or semiocclusive dressings • Autolytically débrides necrotic tissue • Impermeable to bacteria • Not to be used in heavily exudative wounds or over sinus tracts • Manufactured in various shapes, sizes, adhesive properties, and forms, including wafers, pastes, and powders	• Comfeel (Coloplast) • DuoDERM (Convatec) • Exuderm (Medline) • MPM Excel (MPM Medical, Irving, Texas) • Primacol (Dumex Medical) • Restore (Hollister, Libertyville, Ill.) • 3M Tegasorb (3M Healthcare)
Enzymatic débriding agents	• Remove devitalized tissue • Can be used to epithelialize areas of skin grafts that did not take (Panafil, Gladase) • Target tissue as a proteolytic, collagenase, or fibrinolytic	• Accuzyme (Healthpoint) • Collagenase Santyl (Ross Laboratories, Ethezyme, Ethex Corp., St. Louis, Mo.) • Gladase-C (Smith & Nephew) • Panafil (Healthpoint)
Antimicrobials	• For use in critically colonized or infected wound beds • Choice to be determined by quantitative biopsy or culture • Most have broad-spectrum coverage • Combinations of ointments, creams, and silver-based dressings can be used	• Cadexomer iodine (Iodosorb/Iodoflex; Smith & Nephew) • Gentamicin (Garamycin 1%) • Mafenide acetate (Sulfamylon 5%; Bertek Pharmaceuticals, Inc., Morgantown, W.Va.) • Metronidazole (Flagyl/Metrogel 0.8%; Gladerma, Fort Worth, Texas) • Mupirocin (Bactroban 2%; GlaxoSmithKline, Research Triangle Park, N.C.) • Silver sulfadiazine (Silvadene 1%; King Pharmaceuticals, Inc., Bristol, Tenn.)

Table 1. ***Continued***

Type of Dressing	Characteristics	Commercially Available Products
Silver ion-impregnated dressings	• Ideal as an antimicrobial barrier to prevent critical colonization of the wound beds • Instantly kill a broad spectrum of bacteria • Can deliver silver instantly to the wound bed (0.5% silver nitrate) or slowly in a sustained-release form (up to 7 days) • Resistance to silver is not a problem • Silver has been shown to affect keratinocytes and should only be used on colonized or infected wounds	• Acticoat Absorbent, Burn, 7day, Moisture Control (Smith & Nephew) • Actisorb (Johnson & Johnson Wound Management) • Arglaes (Medline) • Aquacel Ag (Convatec) • Contreet (Coloplast) • Silvasorb (Medline) • Silverlon Pad, Tubular Stretch, Wound and Burn Contact Dressings, and Packing Strip (Argentum Medical, Willowbrook, Ill.)
Antiseptics	• Unselective in their effect • Destroy both bacteria and local tissue • Can be used as a rinse	• Acetic Acid 0.25% • Chlorhexidine • Dakin's Solution 0.5% • Gentian Violet • Iodine
Impregnated gauze	• Woven or nonwoven materials in which substances have been incorporated into the dressing material by the manufacturer • Maintain moisture in the wound bed • Act as nonadherent primary dressings • Can prevent sutures from "snagging" on gauze	• Adaptic nonadhering dressing (Johnson & Johnson Wound Management) • Scarlet Red Ointment Dressing (Tyco Healthcare/Kendall) • Xeroform (Tyco Healthcare/Kendall)
Other	• Topical PDGF • Silicone nonadherent mesh • MMP binder • MMP binder with silver • Capillary bed stimulant that also improves epithelialization and promotes healing	• Becaplermin (Regranex 0.01% gel; Johnson & Johnson Wound Management) • Mepitel (Molnlycke) • ORC/Collagen (Promogran; Johnson & Johnson Wound Management) • ORC/Collagen with silver (Prisma; Johnson & Johnson Wound Management) • Xenaderm (Healthpoint)

PDGF, platelet-derived growth factor; MMP, matrix metalloproteinase.

in silver ion-impregnated formulations. They are generally waterproof, which may prevent bacterial and environmental contamination. A few examples that are available in an amorphous gel are Curasol (Healthpoint), Intrasite (Smith & Nephew, Largo, Fla.), and Skintegrity (Medline Industries, Mundelein, Ill.). Silvasorb (Medline) is a hydrogel with silver ions; it may be used in a previously heavily colonized wound bed that is beginning to progress through the stages of healing. It is available as an amorphous gel, as a cavity filler, and in sheet form, depending on the size of the wound bed; the latter is more cost effective for large wounds (>3.0 × 3.0 cm).

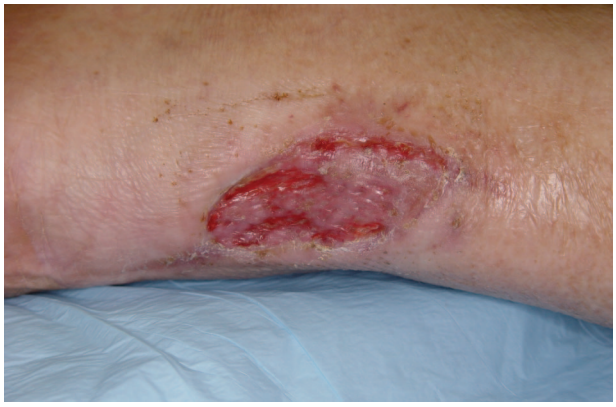

Fig. 24. This wound is well on its way to closing, with pink neoepithelium ingrowth from the periphery.

Transparent films are adhesive, semipermeable, polyurethane membrane dressings that allow for observation of the wound bed. They are waterproof and impermeable to bacteria and contaminants, yet they permit water vapor to cross the barrier.[76] They should not be used on fragile skin or with wounds that have moderate to heavy exudates, since are not absorbent. Examples of transparent films are OpSite (Smith & Nephew), Tegaderm (3M Health Care, St. Paul, Minn.), and Mefilm (Molnlycke, Newtown, Pa.).

Impregnated gauze dressings are woven or nonwoven materials in which substances such as iodinated agents, petrolatum, zinc compounds, and aqueous saline have been incorporated. They maintain moisture in the wound bed, act as nonadherent primary dressings, and can also prevent sutures from "snagging" on gauze. Examples of impregnated gauze dressings are Xeroform (Tyco Healthcare/Kendall, Mansfield, Mass.), Adaptic

nonadhering dressing (Johnson & Johnson Wound Management, Somerville, N.J.), and Scarlet Red Ointment Dressing (Tyco Healthcare/Kendall).

Granulating Wounds

Granulation tissue is a transitional replacement for normal dermis characterized by beefy red tissue that represents an extremely dense network of blood vessels and capillaries (Fig. 25). This eventually matures into a scar during the remodeling phase of healing.

The commonly accepted practice of using normal saline wet-to-dry dressings for granular wound beds has been shown to actually have deleterious effects on healing. Wet gauze dressing can impair wound healing by lowering the wound temperature and impeding fluid evaporation. As described previously, these dressings mechanically débride necrotic as well as healthy tissue, causing injury to the wound and increased pain. Furthermore, when these dressings are removed, bacteria may be aerosolized. Finally, these dressings need to be changed two to three times per day for maximum effectiveness. This may not be cost effective when the expense of the supplies and caregiver costs are calculated.[77]

Granulating wound dressings should provide moisture, maintain physiological temperatures, and establish a bacterial barrier. An occlusive dressing promotes angiogenesis and the more rapid formation of granulation tissue.[78] A wound that heals under moist conditions is less fibrotic and scarred than wounds that heal under dry conditions. Furthermore, occlusive dressings have been shown to decrease pain.[79] In addition to the use of transparent dressings, hydrogels, foams, and hydrocolloids, adjuvants appropriate to this class of wounds include matrix metalloproteinase binders and topical growth factors.

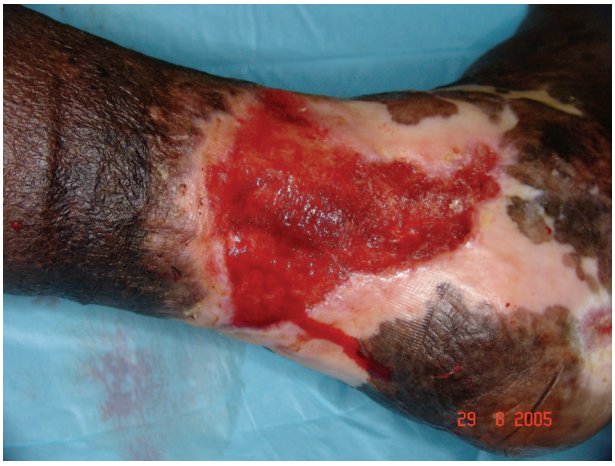

Fig. 25. This wound represents a healthy healing wound with fine, red granulation tissue covering it.

Hydrocolloids are occlusive or semiocclusive dressings composed of materials like gelatin, pectin, and carboxymethylcellulose. They are impermeable to bacteria and other contaminants, are self-adherent, and mold well to the body. They also provide light to moderate absorption of exudates and minimize skin trauma that can disrupt healing. They should not be used on heavily exudative wounds that may dislodge them or wounds with sinus tracts, where they may provide an occlusive environment that limits gas exchange. They are manufactured in various shapes, sizes, adhesive properties, and forms, including wafers, pastes, and powders. Comfeel (Coloplast, Marietta, Ga.), DuoDERM (Convatec, Skillman, N.J.), Exuderm (Medline), MPM Excel (MPM Medical, Irving, Texas), Primacol (Dumex Medical, Toronto, Canada), Restore (Hollister, Libertyville, Ill.), and 3M Tegasorb (3M Healthcare) are various forms of hydrocolloid dressings.

Matrix metalloproteinase binders and topical growth factors should be considered on a clean granulating wound that is not showing signs of progressing toward healing, as evidenced by decreasing in size 10 to 15 percent per week. Matrix metalloproteinases are an important class of proteases involved in extracellular matrix remodeling. In delayed wound healing, there seems to be an overproduction of matrix metalloproteinases, leading to wound degradation and an increased inflammatory state. Inhibiting matrix metalloproteinase activity should therefore permit growth factor activity to allow the progression of wound healing. This can be achieved by applying a sterile, freeze-dried composite of 45% oxidized regenerated cellulose (ORC) and 55% collagen (Promogran; Johnson & Johnson Wound Management). In the presence of wound exudates, it transforms into a soft, conforming, biodegradable gel matrix to which proteases (matrix metalloproteinases) are bound and inactivated. In addition, growth factors are bound and subsequently released in an active form as the dressing undergoes biodegradation. In a previously colonized wound bed, ORC/Collagen with silver (Prisma; Johnson & Johnson Wound Management) is a better choice to achieve stabilization of matrix metalloproteinases antimicrobial properties.

Transforming growth factors are proteins that mediate cellular functions leading to wound healing. Of the multitude of transforming growth fac-

tors in the wound-healing cascade, only Regranex (becaplermin gel 0.01%; Johnson & Johnson Wound Management), a platelet-derived growth factor, is approved by the U.S. Food and Drug Administration for the treatment of diabetic foot ulcers. Becaplermin can be used synergistically with ORC/Collagen to promote wound healing.

Exudative Wounds

Exudative wounds are observed for the amount of fluid released (minimal, moderate, or high) (Fig. 26). A sudden increase in the amount or type of exudate warrants an investigation for a deep infection or pocket of devitalized tissue that is not visible on the surface of the wound bed. This fluid may also be harmful to the periwound tissue by causing maceration; thus, proper management of the moderate to highly exudative wound bed involves absorption of excess fluid.

Foams are hydrophilic polyurethane/polymer or gel-coated dressings that support autolytic débridement in wounds that are minimally to moderately exudative. These dressings maintain a moist wound environment, insulate the wound, and are nonadherent, allowing atraumatic removal. Foams should not be used on dry eschar and do not prevent periwound maceration in heavily exudative wounds. They are available as pads, sheets, and cavity dressings. Examples include Allevyn (Smith & Nephew), Curafoam (Tyco Healthcare/Kendall), Lyofoam (Convatec), Mepilex Border (Molnlycke), Optifoam (Medline), Polymem (Ferris Manufacturing Corp., Burr Ridge, Ill.), and Tielle (Johnson & Johnson Wound Management). Foams can be changed daily or left in place for up to 7 days when used in conjunction with multilayered compression dressings.

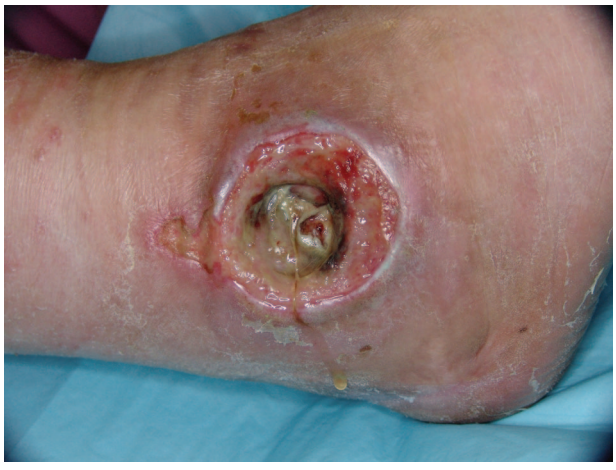

Fig. 26. A necrotic infected wound with serous exudates tracking from the necrotic tissue onto normal skin. Over time, this can lead to maceration and increased wound size.

Alginates are derived from brown seaweed and are composed of soft, nonwoven fibers shaped as ropes or pads, which are able to absorb up to 20 times their weight. They are also hemostatic,[80] biodegradable, mildly antibacterial,[81] and nonantigenic. They form a gel that maintains a moist wound-healing environment and are indicated for wounds with moderate to heavy exudates. They are ideal dead space fillers and may also be used in tunneling wounds. Alginates combined with silver are effective on infected wounds. Alginates are contraindicated in minimally exudating wounds, since they can dehydrate the wound bed. Algicell (Dumex), Algisite (Smith & Nephew), Carrasorb (Carrington Laboratories, Irvin, Texas), Curasorb (Tyco Healthcare/Kendall), Kalginate (DeRoyal, Powell, Tenn.), Kaltostat (Convatec), Maxorb (Medline), SeaSorb (Coloplast), and Sorbsan (Bertek Pharmaceuticals, Morgantown, W.Va.) are various kinds of alginates. Hydrofibers (Aquacel; Convatec) are a subset of alginates that are 30 percent more absorptive but do not wick the exudates away from the wound bed as effectively. They are an ideal skin graft donor-site dressing. Aquacel AG (Convatec) and Silvercel (Johnson & Johnson Wound Management) are preparations that contain silver and can be used for exudative, infected wounds.

Macerated and dehisced incisions can be treated using cadexomer iodine, a versatile product that cleanses the wounds by absorbing pus, fluid, exudates, bacteria, enzymes, and cellular residue. It is available as both a gel (Iodosorb; Healthpoint) and a pad (Iodoflex; Smith & Nephew). It can be applied daily or left on wound beds for up to 7 days. When the dressing color changes from orange-brown to yellowish gray, the dressing should be reapplied. It is contraindicated in patients with iodine allergies or thyroid disease.

Fibrinous Wounds

Fibrin is a natural byproduct of proteins that develops in wound beds. If it is left in place, it can delay wound healing by blocking the formation of granulation tissue (Fig. 13, *below, left*). It can also lead to excess matrix metalloproteinases, increasing the inflammatory status of a wound and leading to cessation of healing. Fibrin is also a great medium for bacteria proliferation. Once this fibrinous protein layer is in place, it needs to be débrided surgically or enzymatically. Enzymatic

débridement can be accomplished autolytically with an occlusive or semiocclusive dressing, such as a hydrogel, hydrocolloid, or transparent film dressing, or with topical enzymatic débriding agents.

Enzymatic débriding agents are effective in removing devitalized tissue from wound beds. The enzymes are categorized as proteolytics, fibrinolytics, and collagenases, depending on the type of tissues that are targeted. The enzyme collagenase digests collagen in necrotic tissue. Collagenase Santyl (Healthpoint) is generally well tolerated by patients and should be applied daily. Papain is a proteolytic enzyme that acts as a potent digestant of nonviable protein matter but is harmless to viable tissue. Adding urea to papain doubles the digestive capabilities. Chlorophyllin copper complex adds healing action to the cleansing action of the papain-urea combination. Patients occasionally complain of a burning sensation in the wound bed because of the urea. Diluting the enzymatic débriding agent with hydrogel may relieve this discomfort. Panafil (Healthpoint) and Gladase-C (Smith & Nephew) are papain-urea-copper-chlorophyllin ointments, but the most potent enzymatic débriders are Accuzyme (Healthpoint) and Ethezyme (Ethex Corp., St. Louis, Mo.). Composed of papain and urea, they digest necrotic tissue and cause liquefaction of pus in acute and chronic wounds. Papain and copper are inactivated when used in conjunction with dressings containing silver ions and hence should not be used in combination.

Infected or Critically Colonized Wounds

By definition, open wounds are contaminated, meaning that the bed contains bacteria that are not actively replicating. This is considered normal and should allow progression of healing. The next pathological step in open wounds is colonization, which is characterized by the replication of microorganisms on the wound surface without invasion of wound tissue and no host immune response. Colonized wound beds are also considered healthy and usually continue to progress through the normal stages of wound healing. Critical colonization refers to a condition in which the bacterial bioburden in the wound reaches a level that interferes with healing but does not produce the classic signs and symptoms of infection. At some point, all colonized wounds run the risk of becoming *critically* colonized. While classic signs of infection may not be present, symptoms such as delayed healing, increased pain/tenderness, increased exudate, abnormal odor, or abnormal or friable granulation tissue might signal critical colonization.

Wound infection is characterized by the presence of replicating microorganisms within a wound, resulting in a subsequent host response such as erythema, warmth, swelling, pain, odor, and purulent drainage (Fig. 27). If not recognized and treated, it possesses the ability to spread systemically, with fever, an elevated white blood cell count, and possibly sepsis. The threshold between colonization and infection may be minute, so early identification and action are critical to healing wounds and minimizing complications. Quantitative research has shown that when the bacterial count (bioburden) reaches levels more than 10^5 bacteria per gram of tissue, it can cause wound infection and inhibit the wound-healing process.[82] Proper topical antibiotics have been shown to decrease the bacterial count (bioburden) of a wound that is showing poor healing secondary to infection or critical colonization.[82,83]

Antiseptics should be avoided in clean wounds, because they are unselective in their effect and destroy both bacteria and the local tissue.[84] Antiseptics include iodine, peroxide, hy-

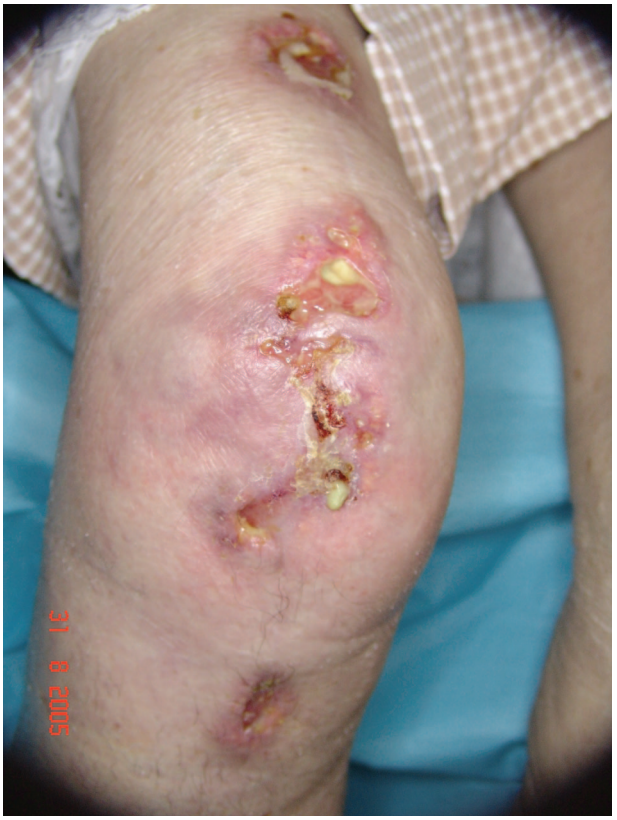

Fig. 27. An infected wound with pus oozing from an opening.

pochlorite, chlorhexidine, boric acid, alcohol, hexachlorophene, Merthiolate, gentian violet, and permanganate. In addition, antiseptic solutions are often ineffective[85] in controlling bacteria, because they bind to the organic material and thus minimize their bactericidal effect. Their usefulness (more specifically, Dakin's solution)[86] has only been demonstrated in dirty open war wounds, in which they primarily functioned to dissolve necrotic tissue. Dilute acetic acid (vinegar) is primarily effective against Gram-negative organisms, such as *Pseudomonas*.[87,88] However, it should only be used to wet dressings and the dressings should not be allowed to dry. An alternative is a silver-containing dressing.

Numerous topical antibiotic ointments and creams can be used in wound care. Mupirocin (Bactroban; GlaxoSmithKline, Research Triangle Park, N.C.) has good coverage against *Staphylococcus*, although resistance develops quickly.[39] Gentamicin is efficacious against *Pseudomonas*. Cadexomer iodine (Iodosorb, from Healthpoint, or Iodoflex, from Smith & Nephew) is effective in a broad-spectrum capacity; it is also offered both as a gel (Iodosorb) and a pad (Iodoflex). Silver sulfadiazine (Silvadene; Aventis) has broad antibacterial properties,[6,7] but caution should be used in patients with sulfa allergies. Antimicrobial ointments or creams should be applied at least once daily to wound beds.

Over-the-counter antimicrobials, such as Bacitracin and Neosporin, are also used frequently. However, both have been implicated as a major source of contact dermatitis and possibly may promote *Pseudomonas* overgrowth. Their use should be discouraged, especially in patients with long-term wounds.

Odoriferous and fungating wounds, often caused by neoplasm or infection, present a special challenge in dressing selection (Fig. 28). It is important to ascertain whether the odor is related to the dressing interacting with exudates. Odor can indicate a need to change the dressing more frequently. If *Pseudomonas* is present, 0.25% acetic acid can alleviate odors. In addition, charcoal has the ability to bind toxins and odor-causing molecules. Actisorb (Johnson & Johnson Wound Management) is a combination of silver and activated charcoal that can be used in chronic wounds. CarboFlex Odor Control (Convatec) is a sterile nonadhesive dressing with an absorbent wound contact layer (containing alginate and hydrocolloid), an activated charcoal central pad, and a smooth water-resistant top layer. Topical Flagyl (metronidazole) is also effective at reducing odor and controlling wound bed bacteria.

Necrotic Wounds

Hydrocolloids, enzymatic débriding agents, antimicrobials, and antiseptics have been implemented in treating necrotic wounds. The amount of necrotic tissue present in the wound bed should drive the dressing selection. Slough is described as

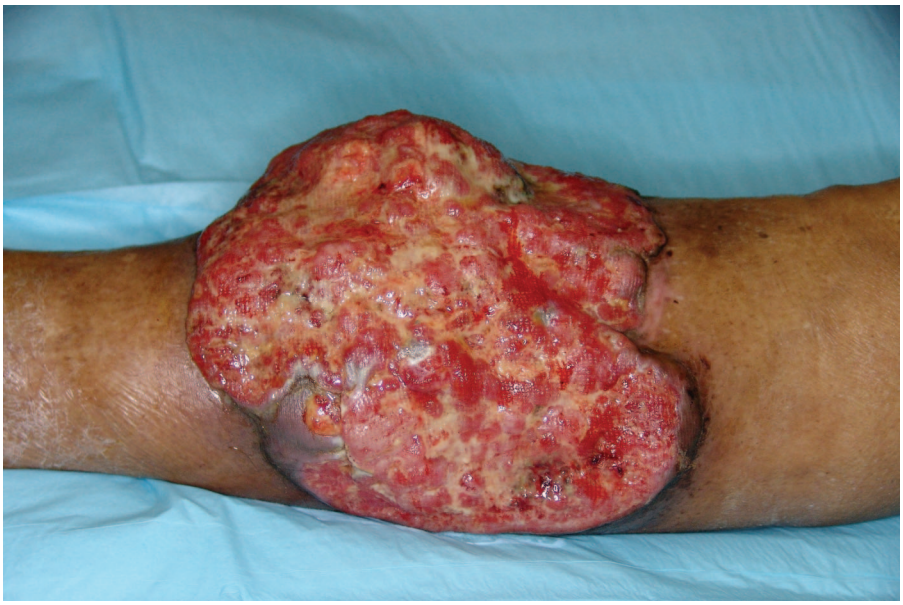

Fig. 28. A wound with exuberant granulating tissue due to a fungating squamous cell carcinoma.

devitalized connective tissue that is moist, stringy, and yellow (Fig. 13, *above, left and center*). The best treatment option is sharp débridement. Eschar appears thick, leathery, and black (Fig. 17, *above, left*). If the eschar is liquefied at the edges or soft in the center, it should be débrided. Mafenide acetate (Sulfamylon; Bertek Pharmaceuticals) is able to penetrate eschar and provide bactericidal properties to the tissue under the eschar. Hypergel (Molnlycke) is a hypertonic 20% saline gel that also penetrates eschar, but it does not have any bactericidal advantages. However, if the eschar covers the entire wound and is dry, it may not be advisable to remove it, as that can destroy the framework of underlying healing.

NEGATIVE PRESSURE WOUND THERAPY

Negative pressure wound therapy (see "Vacuum-Assisted Closure: State of Basic Research and Physiologic Foundation," by Morykwas et al., and "Vacuum-Assisted Closure: State of Clinic Art," by Argenta et al., both in this issue) consists of placing an open cell sponge directly on the wound surface and covering it with an occlusive film. "Negative" pressure is applied to the entire wound surface. (There is no such thing as negative pressure in physics. The pump merely lowers the pressure to below that of ambient pressure, so that the sponge contents move toward the pump.) The "negative" pressure can be either constant or intermittent, and although the recommended pressure is 125 mmHg, it can go as high as 175 mmHg. The "negative" pressure not only decreases the bacterial wound count but also stimulates the rapid formation of granulation tissue.[11,12] The mechanisms that cause the negative pressure wound therapy device to stimulate the formation of granulation tissue are not fully understood. Some posit that the induced changes in the cytoskeleton trigger cell duplication.[89–91] Constant suction of the wound surface may remove a sufficient concentration of factors inhibiting local wound healing (proteases such as matrix metalloproteinase-8 and elastases) that the balance of growth factors to proteases is altered in favor of the former. The reduction of surrounding edema and the resultant improved blood flow, as well as the lower bacterial count, also contribute to the rapid formation of granulation tissue.

The negative pressure wound therapy device can be applied over any type tissue, including dermis, fat, fascia, tendon, muscle, blood vessels, and bone, and hardware.[25] There are two important prerequisites: that the wound be free of gross infection and necrotic tissue and that the wound be well vascularized (necrosis can occur when the pressure device is placed on an ischemic wound). To avoid the risk of a deeper infection, the wound *should be completely débrided to clean tissue* before the device is applied. A thin permeable dressing capable of leeching out silver ions can be placed between the wound and the sponge to help suppress bacterial growth [Acticoat (Smith & Nephew, Hull, United Kingdom) and Silverlon (Argentum Medical, LLC, Chicago, Ill.)]. Pain can sometimes be a limiting factor, especially when the sponge is changed. Applying a lower pressure and inserting an intervening nonadherent woven gauze, such as Adaptic or a silicone-perforated sheet (Mepitel; Mölnlycke Health Care AB, Göteborg, Sweden), can sometimes mediate that pain.

The negative pressure wound dressing is an excellent initial dressing after wound débridement because it decreases edema as well as the local bacterial count. It is an excellent temporizer because it allows the reconstructive surgeon time before committing to a definite reconstruction. It may also stimulate sufficient granulation tissue to cover or fill in a defect, so that the wound can then be skin grafted. This prolonged application of negative pressure wound therapy can even be used successfully in wounds that have exposed bone or hardware.[25]

GROWTH FACTORS

Clinically, the only growth factor that has been approved for use is recombinant DNA platelet-derived growth factor (see "Clinical Evaluation of the Recombinant Human Platelet-Derived Growth Factor for the Treatment of Lower Extremity Diabetic Ulcers," by Steed, and its Discussion by Mustoe, in this issue). It has been shown to accelerate healing and is effective in diabetic foot ulcers.[92] Its effectiveness, however, is directly related to the cleanliness[8] and vascularity of the wound. If metalloproteases are present on the wound's surface, not only will the growth factor be quickly metabolized but the growth factor cell receptors will be destroyed as well. Therefore, if the growth factor is placed on top of a wound covered with protein coagulum, it will quickly be inactivated and hence become ineffective. It is critical, therefore, to remove the protein coagulum on top of the wound every time the growth factor is applied. This can be done with a small curette or a toothbrush (Fig. 11). If the pain from débriding is excessive, then one can alternate using the growth factor with an autolytic débrider. If growth factor is placed on a wound with a poor vascular blood

supply, the wound will lack the building block necessary for the growth factor to have much of an effect.

Growth factor should only be applied if the wound is not healing at the expected rate of 15 percent per week.[62,63,66] Growth factor should not be used unless the wound is clean and has a good blood supply, and it should only be placed on an area where the biomechanical abnormalities that caused the initial wound have been corrected. Therefore, if a plantar forefoot wound occurred because of a tight Achilles tendon, then the Achilles tendon should be lengthened before any decision is made as to whether growth factor is needed or not.[21–23] Finally, combining hyperbaric oxygen and growth factor speeds up healing more than either adjunct alone in a trial performed on rabbit ears.[93] The same results were absent in aged rabbit ears, suggesting that the age of the host may affect the process. Clinical human trials are currently underway to see whether there is an added benefit to combining hyperbaric oxygen with growth factor (Fig. 16).

SKIN SUBSTITUTES

Skin substitutes are very useful in assessing the quality of a wound bed as well as possibly converting a hostile, stagnant, or nonhealing bed into a healthy one (see "The Efficacy of Apligraf in the Treatment of Diabetic Foot Ulcers," by Dinh and Veves, its Discussion by Armstrong, and "Reconstructive Surgery with Integra Dermal Regeneration Template: Histologic Study, Clinical Evaluation, and Current Practice, by Moiemen et al., in this issue). The incorporation of processed skin grafts, such as xenograft (pigskin) [94,95] or allograft, by a wound bed demonstrates that it has adequate blood supply and a sufficiently low bacterial count to allow an autograft to heal successfully. Living skin equivalents can also be used to convert the wound bed into a healthy bed by stimulating the production of growth factors to stimulate the wound to heal. Living skin equivalents act as a biologically active dressing and should only be considered for use on an adequately débrided wound.

Xenografts are made from porcine skin, and their success is thought to be due to their underlying collagen matrix.[96,97] If the skin bed has been well prepared, it takes similarly to a skin graft, with neovascularization occurring 4 to 6 days after being applied, when the pale graft assumes a pinkish hue. Depending on the immune status of the patient, rejection will begin anywhere from 9 to 45 days later. A xenograft that has taken can then be replaced with an autologous skin graft with a very high degree of success. Xenografting is therefore used clinically to assess the suitability of a given recipient bed for a skin autograft, because a failed skin graft with its donor site is a serious problem, especially in the elderly or immunocompromised patient.

An allograft[98] (preserved cadaver skin) can be used in the same way as a xenograft. It is likewise rejected depending on its antigenicity and the patient's immune status. Its availability is far more limited and its cost is far higher than those of xenografts, and there is also the potential concern of disease transmission. However, both xenografts and allografts have proven to be extremely useful in the treatment of burn patients,[99] by accelerating healing and minimizing scarring.

Engineered skin substitutes, consisting of a collagen matrix, initially function similarly to xenografts and allografts, but because they lack antigenicity, they become integrated in the underlying wound and do not stimulate rejection. Integra artificial skin (Integra Lifesciences Holding Corp., Plainsboro, N.J.) is composed of an overlying removable silicone film (to prevent desiccation) with an underlying dermal matrix of cross-linked bovine collagen and chondroitin sulfate.[100,101] The dermal layer functions as a dermal template to facilitate angiogenesis as well as a scaffold for the migration of the patient's own fibroblasts, macrophages, lymphocytes, and endothelial cells. Over the ensuing weeks, a new cell-populated dermis is formed.[102,103] This process can be rapidly accelerated (7 to 10 days) by applying the negative pressure wound therapy device on top of the silicone sheet.[104,105] The silicone layer can then be removed so that a very thin skin autologous skin graft (6/1000ths to 12/1000ths of an inch) can be placed on the wound.[106] Integra has been effective in burn wounds[107] and in reconstructive surgery.[103] AlloDerm (LifeCell Corp., Branchburg, N.J.) is an acellular allograft made of cryopreserved cadaver skin. It consists of a decellularized dermal matrix with a structurally intact dermis and basement membrane. The freeze-dried dermis has to be rehydrated with sterile saline. It is placed on the wound bed and can be immediately covered with a thin autograft. In a single trial, it was shown to function almost as well as a thick skin graft.[108] In this instance, however, the quality of the recipient wound bed has to be equal to that on which an autograft would be placed. It is now also being used increasingly as a substitute mesh in repairing trunk wall defects.[109] Finally, TransCyte (Smith & Nephew) is a bioengi-

neered dermis consisting of cultured human newborn fibroblasts on a nylon mesh coated with porcine dermal collagen and bonded to a silicone membrane to provide a moisture vapor barrier. After the fibroblasts have secreted dermal collagen, matrix protein, and growth factor, the construct is then frozen so that no metabolic activity remains. This has been proven to be an effective dressing for partial-thickness burns.[110–112]

Apligraf (Organogenesis, Inc., Canton, Mass.) consists of a bovine collagen matrix seeded with human dermal fibroblasts and epidermal keratinocytes from neonatal foreskin tissue. They, in turn, form a living bilayered construct that mimics human skin. Apligraf effectively stimulates the formation of granulation tissue and neoepithelialization by acting as a local producer of the necessary growth factors and wound-healing adjuncts. In about 10 to 15 percent of cases it actually appears to behave much like a normal skin graft, although the final epithelium is only from the host.[113] It has been shown to be effective in promoting healing in randomized trials in venous stasis ulcers[114] and diabetic foot ulcers.[115] For it to be successful, it has to be placed on a clean, healthy wound surface.

Dermagraft (Smith & Nephew), a polyglycolic mesh infiltrated by dermal fibroblasts, has been used successfully to treat diabetic foot ulcers[116,117] and venous stasis ulcers.[118] Dermagraft's effectiveness is based on its ability to secrete the appropriate growth factors. As of January of 2006, it is no longer available in the United States. OrCel is also a bilayered product available[119] in Europe and being tested in the United States. It likewise consists of dermal scaffolding populated by fibroblasts and an epithelial layer with keratinocytes. It has been shown to be effective on donor sites in burn patients.[120] Its mode of effectiveness is again thought to be due to its ability to locally produce the necessary growth factors to stimulate normal wound healing.

HYPERBARIC OXYGEN

Oxygen is an essential component of wound healing, and the wound's ability to heal can be directly linked to the level of tissue oxygenation (see "Using Physiology to Improve Surgical Wound Outcomes," by Ueno et al., in this issue).[121] Oxygen is used for protein synthesis, cell replication, hydroxylation of collagen, exportation of collagen out of the fibroblast cell, and neoepithelialization.[122,123] The strength of the subsequent wound repair is related to oxygen concentration.[124,125] Angiogenesis at the wound's edges is driven by the existing oxygen gradient[126] from the center of the wound, which is oxygen-poor while the periphery is oxygen-rich. The resultant oxygen-poor, lactate-rich gradient drives macrophages to produce angiogenesis factors until capillary ingrowth is complete. The periphery of the wound supplies the necessary oxygen to support the process. Furthermore, the leukocyte's ability to kill bacteria is in part based on its ability to produce free radicals, which is oxygen gradient dependent.[127] This gradient also affects the leukocyte's ability to clear bacteria from the wound site.[128]

Because skin and connective tissue are under the control of the autonomic system, blood flow and resultant oxygen delivery are affected by pain, cold, and decreased blood volume. [129,130] Therefore, simple measures, such as controlling pain, keeping the environment warm, and maintaining adequate fluid volume, can optimize oxygen delivery to the wound site. Drugs such as nicotine may negatively affect the autonomic system and diminish local blood flow to the wound site. Measuring the tissue oxygen level around the wound is the most accurate way to assess immediate wound perfusion.[131] Elevating the leg above the heart decreases blood flow by 20 percent for each 10 cm of elevation. Dangling a limb over the side of a bed, often seen in patients with rest pain, increases the transcutaneous oxygen level by 22 mmHg. Adding nasal oxygen can further increase the transcutaneous oxygen level by an additional 12 mmHg.[132] and it also decreases the risk for wound infection in the surgical patient.[133]

Systemic hyperbaric oxygen further increases tissue oxygenation. The treatment consists of pressurizing the patient in a chamber to pressures greater than 1 atmosphere and adjusting the surface breathing mixtures to 100% oxygen. Each gram of hemoglobin carries 1.34 ml of bound oxygen, while inhaled air only adds 0.3 cc of dissolved oxygen per 100 cc of blood. This means that someone with a hemoglobin level of 15 who is breathing normal air carries 20.1 cc of oxygen (15 × 1.34) via hemoglobin. He or she also carries 0.33 cc of dissolved oxygen in the surrounding plasma for a total of 20.4 cc per 100 ml. Hyperbaric oxygen further increases the amount of dissolved oxygen, so that each additional atmosphere of pure oxygen adds 2.2 cc of dissolved oxygen per 100 cc of blood (2.2 vol. %).

Because the capillaries around a chronic wound are often partially occluded because of the presence of microthrombi, the passage of red blood cells is limited. However, plasma can still flow and the amount of oxygen it carries therefore

becomes very important.[134] Krogh[135] has shown that in these capillaries containing only plasma, the oxygen concentration on the arterial side at 2 atmosphere of oxygen is four-fold that of normal inspired air, while it is two-fold that on the venous side. The dissolved oxygen in the plasma under hyperbaric conditions (2.2 vol. %) meets the oxygen extraction rates of skin (i.e., the oxygen extraction rate of skin is 2.0 vol. % versus 11.0 vol. % for the heart, 6.1 vol. % for the brain, and 5.0 vol. % for muscle).[136] Obviously, for hyperbaric oxygen treatments to be effective, the circulation bringing blood to the wound periphery has to be patent.

Clinical studies have shown that hyperbaric oxygen treatments are successful in healing diabetic ulcers[137] (randomized, nonblinded), preventing diabetic amputations[138] (randomized, double-blind), and healing chronic ulcers[139] (randomized, double-blind). Osteoradionecrosis has been treated successfully with hyperbaric oxygen, especially in the jaw.[140,141] Hyperbaric oxygen treatments are likewise effective in limiting tissue damage in more extreme medical emergencies. The treatments minimize tissue necrosis after surgical release of the fascial compartment of limbs suffering from compartment syndrome[142] or in patients with gas gangrene.[143] Hyperbaric oxygen has also been used successfully in reimplantation when there has been a long delay before reimplantation or when there has been extensive trauma involving the reimplanted part. [144,145] Also, hyperbaric oxygen treatments have been used successfully to salvage failing flaps.[146]

The selection of patients who might benefit from hyperbaric oxygen treatment should be very strict. The wound must have failed conservative wound therapy and must not be decreasing in area by the prerequisite 10 to 15 percent per week. The wound must be well vascularized and adequately débrided. The patient must have a transcutaneous oxygen level at the wound periphery measuring less than 40 mmHg. The patient should then be tested for the affected tissue's response to increased inspired oxygen. After the patient has breathed 100% oxygen through a mask, the transcutaneous oxygen level should increase by at least 10 mmHg. Alternatively, if the patient is given a hyperbaric test dive, the transcutaneous oxygen level should increase above 200 mmHg. If the patient fails these tests, then he or she is unlikely to benefit from hyperbaric oxygen therapy.

Each treatment should last for 90 minutes. After treatment, the increased oxygen perfusion persists for 1 hour in muscle and for up to 4 hours in the skin and subcutaneous tissue.[147] The need for supplemental oxygen must be balanced by the risk of oxygen toxicity. Twice-a-day treatments are used acutely for extreme conditions (necrotizing fasciitis, ischemic limb after release of compartment syndrome, radiation burn, and failing flaps). However, for chronic wounds, treatment once a day is sufficient. Adding topical growth factor to the wound during hyperbaric oxygen treatments has been shown in rabbits to affect the wound more than either treatment alone.[93] The wound should then be monitored closely and the hyperbaric treatments can be stopped when the characteristics of the wound have changed to those of an acute wound. At this point, alternative, less expensive strategies can be used, such as conservative dressing regimens, topical growth factor, skin substitutes, and skin grafts.

CONCLUSIONS

Wounds can progress through the normal stages of healing, provided that they are clean, healthy, and maintained in an environment conducive to anabolic metabolism. Débridement is fundamental in achieving these goals, provided that (1) the tissue is well vascularized, (2) antibiotics are administered appropriately, if necessary, and (3) all other medical aspects of the patient have been addressed. Surgical débridement is the quickest and most effective way of preparing the wound for healing. Once a wound bed has been adequately débrided, conservative wound care measures or conventional reconstructive surgical techniques may be employed.

If the wound closure rate is not 10 to 15 percent per week and/or if vital structures (bone, tendon, and neurovascular bundle) are exposed, the wound may require additional measures to promote healing. The negative pressure wound therapy device is an excellent tool that stimulates formation of granulation tissue while decreasing local edema and controlling bacterial proliferation. It has the advantage of speeding the wound-healing process by secondary intention and can make a larger wound more amenable to simpler reconstructive techniques. Other modalities that stimulate the formation of granulation tissue and speed up wound closure include topical growth factor, bioengineered skin substitutes, and hyperbaric oxygen. Once the wound has been converted to a healthy acute wound with a closure rate of 10 to 15 percent per week, one can either change to a moist wound-healing dressing regimen or apply

reconstructive surgical techniques to achieve final closure.

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