7 ACUTE WOUND CARE

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Acute wounds are the result of local trauma and may be associated with severe life-threatening injuries. The approach to a patient with an acute wound begins with assessment of the ABCs (airway, breathing, and circulation). Life-threatening injuries are addressed first. Only after more urgent problems have been corrected is the wound itself addressed. A complete history is obtained and a thorough physical examination is performed, with special attention paid to both local and systemic wound environment factors that may affect healing. Information about the cause of injury is sought. In the case of a hand injury, the patient's hand dominance and occupation are determined. All patients with acute wounds should be assessed for malnutrition, diabetes, peripheral vascular disease, neuropathy, obesity, immune deficiency, autoimmune disorders, connective tissue diseases, coagulopathy, hepatic dysfunction, malignancy, smoking practices, medication use that could interfere with healing, and allergies. The local wound environment should be evaluated to determine the extent and complexity of injury, the tissues involved, the degree of contamination by microorganisms or foreign bodies, and the extent of damage related to previous irradiation or injury to surrounding tissues.

The wound is carefully examined, with particular attention paid to size, location, bleeding, arterial or venous insufficiency, tissue temperature, tissue viability, and foreign bodies. Latex- and powder-free gloves are worn to prevent allergic reactions, and a shielded mask should also be used to protect the practitioner from body fluids.[1] The possibility of damage to vessels, nerves, ducts, cartilage, muscles, or bones in proximity to the injury is assessed. X-rays and a careful motor and sensory examination may be required to rule out such injuries. While these tests are being performed, moist gauze should be applied to wounds to prevent desiccation.

The goal of acute wound management is to create a healing wound that will result in the best functional and aesthetic outcome. In what follows, we address the key considerations in management of the acute wound, including anesthesia, choice of repair site (e.g., operating room or emergency department), hemostasis, irrigation, débridement, closure materials, timing and methods of closure, adjunctive treatment (e.g., tetanus and rabies prophylaxis, antibiotics, and nutritional supplementation), appropriate closure methods for specific wound types, dressings, postoperative wound care, and potential disturbances of wound healing. We conclude by briefly reviewing the physiology of wound healing.

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Wound Preparation

ANESTHESIA

After conducting a careful motor, sensory, and vascular examination, adequate general or local anesthesia must be instituted before definitive exploration and treatment can begin. General anesthesia in the operating room should be employed in any of the following circumstances: if the patient is unable to tolerate local anesthesia; adequate pain control cannot be achieved with a local block; the wound requires significant débridement, exploration, or repair; bleeding cannot be controlled; or the required local anesthetic dose for adequate pain control exceeds the maximum safe dose. Local anesthesia is usually sufficient for débridement and closure of most small traumatic wounds. Often the local anesthetic may be injected directly into wounded tissue. However, direct wound injection may be less reliable in inflamed or infected tissue or may distort important anatomic landmarks used to align wound edges. In these situations, regional nerve blocks directed at specific sensory nerves outside the injured field may be employed instead.

Injectable anesthetics can be broadly divided into amides and esters [*see Table 1*]. An easy way to remember which category an agent belongs to is to recall that the amides all have two i's in their generic name, whereas the esters have only one. Lidocaine, an amide, is the most commonly used local anesthetic. Its advantages include a rapid onset of action (< 2 minutes), extended duration of effect (60 to 120 minutes), relative safety in comparison with more potent anesthetics (e.g., bupivacaine), and availability in multiple forms (e.g., liquid, jelly, and ointment) and concentrations (e.g., 0.5, 1.0, and 2.0%). In addition, lidocaine rarely causes allergic reactions, whereas ester anesthetics (e.g., tetracaine) are metabolized to para-aminobenzoic acid, which may cause allergic reactions in some patients. Bupivacaine (Marcaine) should be considered when longer periods of anesthesia are desired (e.g., length of action, dosing).

Vasoconstriction can be produced by adding epinephrine to a local anesthetic, usually in a dilution of 1:100,000 or 1:200,000 (5 to 10 μg/mL). Through vasoconstriction, epinephrine prolongs the anesthetic agent's duration of action, allows a larger dose to be safely administered, and aids in hemostasis.[2] Traditionally, local anesthetics with epinephrine have not been used in finger and toe wounds because of the theoretical risk of ischemia and tissue loss. Nevertheless, these adverse effects have not yet been clinically reported or documented by any prospective studies.[3]

Local anesthetics can cause systemic toxicity when injected intravascularly or given in excessive doses. Manifestations of systemic toxicity begin with central nervous system effects (e.g., vertigo, tinnitus, sedation, and seizures) and may progress to cardiovascular effects (e.g., hypotension, cardiac conduction abnormalities, and cardiovascular collapse). Treatment for systemic toxicity is supportive with oxygen, airway support, and cardiovascular bypass (if

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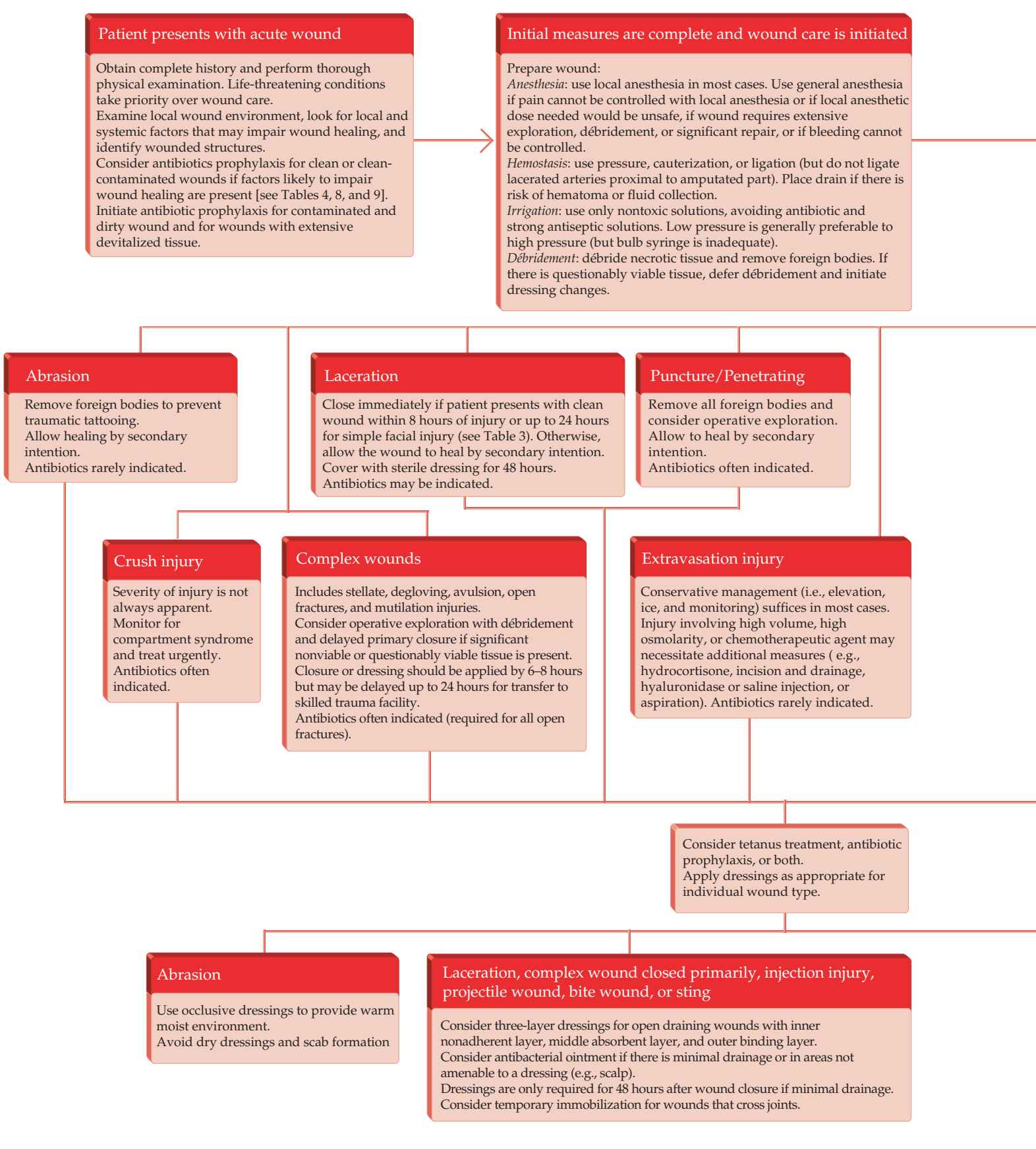
Patient presents with acute wound
Obtain complete history and perform thorough physical examination. Life-threatening conditions take priority over wound care.
Examine local wound environment, look for local and systemic factors that may impair wound healing, and identify wounded structures.
Consider antibiotics prophylaxis for clean or clean-contaminated wounds if factors likely to impair wound healing are present [see Tables 4, 8, and 9].
Initiate antibiotic prophylaxis for contaminated and dirty wound and for wounds with extensive devitalized tissue.
Initial measures are complete and wound care is initiated
Prepare wound:
Anesthesia: use local anesthesia in most cases. Use general anesthesia if pain cannot be controlled with local anesthesia or if local anesthetic dose needed would be unsafe, if wound requires extensive exploration, débridement, or significant repair, or if bleeding cannot be controlled.
Hemostasis: use pressure, cauterization, or ligation (but do not ligate lacerated arteries proximal to amputated part). Place drain if there is risk of hematoma or fluid collection.
Irrigation: use only nontoxic solutions, avoiding antibiotic and strong antiseptic solutions. Low pressure is generally preferable to high pressure (but bulb syringe is inadequate).
Débridement: débride necrotic tissue and remove foreign bodies. If there is questionably viable tissue, defer débridement and initiate dressing changes.
Abrasion
Remove foreign bodies to prevent traumatic tattooing.
Allow healing by secondary intention.
Antibiotics rarely indicated.
Laceration
Close immediately if patient presents with clean wound within 8 hours of injury or up to 24 hours for simple facial injury (see Table 3). Otherwise, allow the wound to heal by secondary intention.
Cover with sterile dressing for 48 hours.
Antibiotics may be indicated.
Puncture/Penetrating
Remove all foreign bodies and consider operative exploration.
Allow to heal by secondary intention.
Antibiotics often indicated.
Crush injury
Severity of injury is not always apparent.
Monitor for compartment syndrome and treat urgently.
Antibiotics often indicated.
Complex wounds
Includes stellate, degloving, avulsion, open fractures, and mutilation injuries.
Consider operative exploration with débridement and delayed primary closure if significant nonviable or questionably viable tissue is present.
Closure or dressing should be applied by 6–8 hours but may be delayed up to 24 hours for transfer to skilled trauma facility.
Antibiotics often indicated (required for all open fractures).
Extravasation injury
Conservative management (i.e., elevation, ice, and monitoring) suffices in most cases.
Injury involving high volume, high osmolarity, or chemotherapeutic agent may necessitate additional measures (e.g., hydrocortisone, incision and drainage, hyaluronidase or saline injection, or aspiration). Antibiotics rarely indicated.
Consider tetanus treatment, antibiotic prophylaxis, or both.
Apply dressings as appropriate for individual wound type.
Abrasion
Use occlusive dressings to provide warm moist environment.
Avoid dry dressings and scab formation
Laceration, complex wound closed primarily, injection injury, projectile wound, bite wound, or sting
Consider three-layer dressings for open draining wounds with inner nonadherent layer, middle absorbent layer, and outer binding layer.
Consider antibacterial ointment if there is minimal drainage or in areas not amenable to a dressing (e.g., scalp).
Dressings are only required for 48 hours after wound closure if minimal drainage.
Consider temporary immobilization for wounds that cross joints.

Approach to Acute Wound Management

Wound is ready for closure

Select closure materials: sutures (see Table 2), staples, tapes, or adhesives.
Determine timing and method of closure (see Table 3):

- Primary intention: clean wound without contraindications to closure
- Secondary intention: wound with contamination or contraindications to closure, wounds with significant amounts of devitalized tissue, wounds older than 8–24 hours, patient who cannot tolerate closure, or wounds for which closure is not needed.
- Tertiary closure: contaminated wound, wound with questionably viable tissue, or patient who cannot tolerate immediate closure
- Skin grafting: large superficial wound
- Tissue transfer: large wound with exposed vital structure

Formulate specific closure approach suitable for individual wound type.

Injection injury

Wound appearance is often deceptively benign.
Examine wound area carefully and obtain appropriate radiographs.
Treat aggressively with incision, wide exposure, débridement, and removal of foreign bodies.
Allow healing by secondary intention.
Antibiotics may be indicated.

Bite wound

Take into account risk of rabies, bacterial and viral infections, and envenomation.
Obtain x-rays to evaluate for fractures and joint involvement.
Treat with exploration, irrigation, débridement, and close observation.
Wounds should be allowed to heal by secondary intention or delayed primary closure except in certain circumstances (e.g., facial wounds).
Consider rabies treatment, rabies prophylaxis, or both (see Tables 6 and 7). Consider antivenom when indicated.
Antibiotics often indicated (see Table 8).

Projectile wounds

Wound appearance is often deceptively benign (high-velocity injuries cause extensive tissue damage).
Foreign bodies are frequently present, and operative exploration is typically required.
Obtain appropriate radiographs.
Wound should be allowed to close by secondary intention or delayed primary closure.
Antibiotics indicated except in soft tissue only injuries.

Stings

Take into account risk of envenomation.
Symptoms may be local or systemic.
Treatment is usually directed toward local symptoms (i.e., analgesia) and wound care.
For systemic reactions, epinephrine, antihistamines, corticosteroids, and supportive care may be required.
The wounded area should be elevated and iced
Antibiotics rarely indicated.

Complex wound left open or closed after delay

Wet-to-dry dressings, wet-to-wet, or negative pressure wound therapy is indicated for contaminated wounds or wounds with questionably viable tissue (negative pressure therapy should not be used over exposed blood vessels or bowel).
Topical antimicrobials may be used in significantly contaminated wounds.
Avoid compression dressings in wounds with questionably viable tissue.

Extravasation injury or crush injury

Avoid compression dressings.

Table 1 Common Injectable Anesthetics[3]

Amides
Lidocaine (Xylocaine)
Bupivacaine (Marcaine)
Mepivacaine (Carbocaine)
Prilocaine (Citanest)
Etidocaine (Duranest)
Phenocaine
Dibucaine (Nupercainal)
Ropivacaine (Naropin)
Levobupivacaine (Chirocaine)
Esters
Procaine (Novocain)
Chloroprocaine (Nesacaine)
Tetracaine (Pontocaine)
Benzocaine (multiple brands)
Propoxycaine (Ravocaine)
Cocaine

necessary) until the anesthetic has been metabolized. The maximum safe dose of lidocaine is 3 to 5 mg/kg without epinephrine and 7 mg/kg with epinephrine. Doses as high as 55 mg/kg have been used without toxicity for tumescent anesthesia in patients undergoing liposuction[4]; however, in this scenario, some of the anesthetic is aspirated by the liposuction lowering the effective dose. The lidocaine doses used for local wound injection should be substantially smaller than those used in liposuction. To prevent local anesthesia from causing systemic toxicity, the recommended safe doses of the anesthetics should not be exceeded and aspiration should be performed before injection to ensure that the agent is not injected intravascularly.

The pain associated with injection of the local anesthetic can be minimized by using a small-caliber needle (27 to 30 gauge), warming the anesthetic, injecting the agent slowly, using a subcutaneous rather than an intradermal injection technique,[5] providing counterirritation, buffering the anesthetic with sodium bicarbonate to reduce acidity (in a 1:10 ratio of sodium bicarbonate to local anesthetic),[6] and applying a topical local anesthetic before injection. Topical local anesthetics (e.g., TAC [tetracaine, adrenaline (epinephrine), and cocaine] and EMLA [a eutectic mixture of lidocaine and prilocaine]) are as effective as injectable anesthetics when applied to an open wound.[7] EMLA requires approximately 60 minutes to induce sufficient anesthesia for open wounds; TAC requires approximately 30 minutes.[8] EMLA is more effective than TAC for open wounds of the extremity. Benzocaine 20% (in gel, liquid, or spray form) can also be used for topical anesthesia and is frequently employed before endoscopic procedures. It is poorly absorbed through intact skin but well absorbed through mucous membranes and open wounds. A 0.5- to 1-second spray is usually recommended, although even with a standardized spray duration, the delivered dose can vary considerably.[9] A 2-second spray results in a statistically, although not clinically, significant increase in methemoglobin levels.[10] Methemoglobinemia is a rare but life-threatening complication of benzocaine spray use. If symptoms of methemoglobinemia develop (e.g., cyanosis or elevated methemoglobin levels on cooximetry), prompt treatment with intravenous (IV) methylene blue, 1 to 2 mg/kg, is indicated.[9]

EXPLORATION

After anesthesia is achieved, the wound should be thoroughly explored. Injuries to the hand should raise a high suspicion for nerve, muscle, tendon, and vascular injuries. In general, complex hand wounds should be explored under tourniquet control in the operating room. Injuries to the abdomen or chest, especially penetrating wounds, should be explored for violation of the abdominal fascia, pleura, or mediastinal spaces. Potential for damage to organs should be assessed, and a low threshold for operative exploration should be maintained. Finally, injuries to the face should elicit high suspicion for nerve (both sensory and motor) or duct injuries (e.g., the parotid duct or the lacrimal duct) that may require probing. Any potential vascular injuries to the extremities should be assessed by measuring an ankle-brachial index (considered abnormal if < 0.9). Radiographs should be obtained to rule out fracture, joint involvement, and embedded foreign material.

HEMOSTASIS

In most wounds, hemorrhage can be readily controlled with pressure, cauterization, or ligation of vessels. Direct pressure with one to two fingers is often all that is needed to stop active bleeding. Avoid placing large amounts of gauze or other absorptive materials on an actively bleeding wound as they may make applying direct pressure difficult and aid little in hemostasis. When direct pressure fails, wound exploration with cauterization or ligation of transected vessels may be appropriate. Lacerated arteries proximal to amputated parts such as fingers or ears, however, should not be ligated because an intact vessel is necessary for microsurgical replantation. In general, vessels greater than 1.5 mm in diameter should be preserved when possible.[11] If ligation is to be performed, the divided end of the vessel should be isolated, clamped with a small hemostat, and ligated with a synthetic absorbable braided suture. Packing, wrapping, and elevating can help control hemorrhage temporarily. If necessary (although the need should be rare, and only in cases of life-threatening hemorrhage), a tourniquet may be applied to an injured extremity. It should be applied before the development of shock. Data from combat situations suggest that survival may be increased and that tourniquet use time of less than 1 hour does not have any significant adverse effects except for transient nerve palsy (rate < 2%).[12]

Hemostasis prevents hematoma formation, thereby decreasing the risk of infection and wound inflammation. If there appears to be a potential risk of hematoma or fluid collection, drains should be placed. Although drains may help prevent accumulation of blood or serum in the wound, they are not a replacement for meticulous hemostasis. Drains facilitate approximation of tissues, particularly under flaps; however, they also tend to potentiate bacterial colonization because they serve as retrograde conduits for bacteria.[13] As a rule, drains can be safely removed when drainage reaches levels of 25 to 30 mL/day. If a hematoma or seroma forms, the subsequent course of action depends on the size of the fluid collection. Small hematomas and seromas usually are reabsorbed and can be treated conservatively. Larger fluid collections provide a significant barrier to healing, and

treatment may include reopening the wound and placing drains. Intermittent sterile aspirations, followed by application of a compressive dressing, may also be indicated.

IRRIGATION

After débridement of necrotic tissue and foreign bodies, the next step is irrigation of the wound. This may be accomplished by several different methods, including bulb syringe irrigation, gravity flow irrigation, and pulsatile lavage. These methods can be further divided into high-pressure (15 to 35 psi) and low-pressure (1 to 15 psi) delivery systems. High-pressure pulsatile lavage may reduce bacterial concentrations in the wound more efficiently than low-pressure and bulb syringe systems,[14] but it can also cause disruption to soft tissue structure and deeper penetration with greater retention of bacteria.[15–17] A recent randomized, controlled trial found no benefit with higher pressures in the irrigation of open fractures, but further studies are needed.[18] In general, low-pressure systems should be employed for acute wound irrigation and high-pressure irrigation may be considered for grossly contaminated wounds. Simply running saline over a wound is of little value; thus, to obtain continuous irrigation with pressures as low as 5 to 8 psi, one group recommended using a saline bag in a pressure cuff inflated to 400 mm Hg and connected to IV tubing with a 19-gauge angiocatheter.[19]

Only nontoxic solutions (e.g., 0.9% sterile saline, lactated Ringer solution, sterile water, and tap water) should be used for wound irrigation.[20] Irrigation with an antibiotic solution appears to offer no advantages over a nonsterile soap solution, and the antibiotic solution may increase the risk of wound-healing problems.[21] Strong antiseptics (e.g., povidone-iodine, chlorhexidine, alcohol, sodium hypochlorite, and hydrogen peroxide) should not be placed directly into the wound because they may impede healing. After copious irrigation, the surrounding skin should be prepared with an antibacterial solution to limit further contamination.

DÉBRIDEMENT

Normal healing can proceed only if tissues are viable, the wound contains no foreign bodies, and tissues are free of excessive bacterial contamination. To reduce the risk of infection, necrotic tissue and foreign bodies must be removed.[22] The wound and the surrounding local tissue must be exposed so that necrotic tissue can be identified and débrided. Hair may be trimmed with scissors or an electric clipper or retracted with an ointment or gel to facilitate exposure, débridement, and wound closure. Close shaving with a razor should be avoided because it potentiates wound infections.[23] Clipping of eyebrows should also be avoided, both because the eyebrows may not grow back and because the hair is necessary for proper alignment.

Some wounds contain a significant amount of questionably viable tissue. Models of wound management have defined three zones of injury: zone of necrosis, zone of stasis (vulnerable to necrosis), and zone of hyperemia (viable tissue).[24] If there is enough indeterminately viable tissue to preclude acute débridement, dressing changes may be initiated. When all necrotic tissue has been surgically or mechanically débrided, the wound can be closed. Adjuncts to help delineate viable tissue include the use of methylene blue to stain tissue, photoplethysmography, laser Doppler ultrasonography, and transcutaneous Po_2 monitoring.[11,25] However, skin usually demarcates by 24 hours and muscle by 4 to 5 days.[17]

Most foreign bodies are easily removed either by hand or surgical débridement. Abrasion injuries or gunpowder explosions can cause small foreign body fragments to embed in and beneath the skin. These small foreign bodies are often difficult to extract but should be removed as soon as possible. Irrigation usually suffices for removal of loose foreign bodies, but surgical débridement with a small drill, sharp instrument, or brush may be required for more firmly embedded material. If the interval between injury and treatment exceeds 1 to 2 days, the wounds will begin to epithelialize and the embedded material will be trapped in the skin, resulting in traumatic tattooing. Although débridement within 6 hours remains the standard of care to decrease the risk of infection, some evidence suggests that débridement can be performed anytime within the first 24 hours if the delay is for the purpose of transferring to an experienced trauma center.[26]

Wound Closure Considerations

MATERIALS

Once the appropriate preparatory measures have been taken (as described above), the wound is ready to be closed. The first step is to choose the material to be used for wound closure. The materials currently available include sutures, staples, tapes, and adhesives. Selection of the appropriate material is based on the type and location of the wound, the potential for infection, the patient's ability to tolerate closure, and the degree of mechanical stress imposed by closure. The selected material must provide wound edge approximation until the tensile strength of the wound has increased to the point where it can withstand the stress present.

The majority of wounds are closed with sutures. A suture is a foreign body by definition; thus, it may generate an inflammatory response, interfere with wound healing, and increase the risk of infection. Accordingly, the number and diameter of sutures used to close a wound should be kept to the minimum necessary for coaptation of the wound edges.

Sutures are categorized on the basis of material, tensile strength, number of filaments, absorbability, and time to degradation [*see Table 2*]. Suture material may be either natural or synthetic. Natural fibers (e.g., catgut and silk) cause more intense inflammatory reactions than synthetic materials (e.g., polypropylene).[27] The tensile strength of suture material is defined as the amount of weight required to break a suture divided by the suture's cross-sectional area. It is typically expressed in an integer-hyphen-zero form whereby larger integers correspond to smaller suture diameters (i.e., 3-0 sutures have a greater diameter and more tensile strength than 5-0 sutures).[28] To minimize the amount of foreign body in the wound and to minimize damage to local tissue, suture of the narrowest diameter with sufficient strength should be used and buried sutured knots should be cut short.[29]

Table 2 Types and Characteristics of Suture Material Used for Wound Closure

Suture Type	*Material*	*Comment*	*Configuration*	*Method of Absorption*	*Tensile Strength at 2 wk (%)*	*Time to Degradation*
Absorbable	Plain catgut (bovine intestinal serosa)	Natural; high tissue reactivity	Monofilament	Proteolysis	0	10–14 days
	Chromic catgut (bovine intestinal serosa treated with chromic acid)	Natural; stronger, less reactive, and longer-lasting than plain catgut	Monofilament	Proteolysis	0	21 days
	Fast-absorbing catgut	Natural	Monofilament	Proteolysis	0	7–10 days
	Polyglytone 6211 (Caprosyn)	Synthetic	Monofilament	Hydrolysis	10	56 days
	Glycomer 631 (Biosyn)	Synthetic	Monofilament	Hydrolysis	75	90–110 days
	Polyglycolic acid (Dexon)	Synthetic	Monofilament/ multifilament	Hydrolysis	20	90–120 days
	Polyglactic acid (Vicryl)	Synthetic	Multifilament	Hydrolysis	20	60–90 days
	Polyglyconate (Maxon)	Synthetic	Monofilament	Hydrolysis	81	180–210 days
	Polyglycolide (Polysorb)	Synthetic	Multifilament	Hydrolysis	80	56–70 days
	Polydioxanone (PDS)	Synthetic	Monofilament	Hydrolysis	74	180 days
	Polyglecaprone 25 (Monocryl)	Synthetic	Monofilament	Hydrolysis	25	90–120 days
	Polyglactin 910 (Vicryl RAPIDE)	Synthetic	Multifilament	Hydrolysis	0	7–14 days
Nonabsorbable	Polybutester (Novafil)	Synthetic; low tissue reactivity; elastic; good knot security	Monofilament	—	High	—
	Nylon (Monosof, Dermalon, Ethilon)	Synthetic; low tissue reactivity; memory effect necessitates more knots	Monofilament	—	High	—
	Nylon (Nurolon)	Synthetic; low tissue reactivity	Multifilament	—	High	—
	Nylon (Surgilon)	Synthetic; silicon coated; low tissue reactivity	Multifilament	—	High	—
	Polypropylene (Prolene, Surgilene, Surgipro)	Synthetic; low tissue reactivity; slippery	Monofilament	—	High	—
	Polyethylene (Dermalene)	Synthetic	Monofilament	—	High	—
	Stainless steel	Lowest tissue reactivity of all sutures; poor handling; creates artifact on CT scan; moves with MRI	Monofilament/ multifilament	—	Highest	—
	Cotton	Natural	Multifilament	—	—	—
	Silk (Sofsilk)	Natural; high tissue reactivity; good knot security	Multifilament	—	Poor	—
	Polyester (Dacron, Mersilene, Surgidac)	Synthetic; uncoated; high friction; low tissue reactivity; poor knot security	Multifilament	—	High	—
	Polyester (Ticron)	Synthetic; silicon coated; low tissue reactivity; good knot security	Multifilament	—	High	—
	Polyester (Ethibond)	Synthetic; polybutylate coated; low tissue reactivity; good knot security	Multifilament	—	High	—
	Polyester (Ethiflex, Tevdek)	Synthetic; Teflon coated; low tissue reactivity; good knot security	Multifilament	—	High	—

CT = computed tomographic; MRI = magnetic resonance imaging.

Suture material may be composed of either a single or multiple filaments. Multifilament suture material may either be twisted or braided, which is of clinical importance because the interstices created by braiding may harbor organisms and increase the risk of infection. Monofilament sutures require five knots for security, whereas multifilament sutures are easier to handle and require only three knots. With all sutures, the knots must be square to be secure and must be tight enough only to coapt the wound edges.

Absorbable or nonabsorbable sutures may be appropriate depending on the situation. Absorbable sutures (lose tensile strength within 60 days) are generally used for buried sutures to approximate deep tissues (e.g., dermis, muscle, fascia, tendons, nerves, blood vessels), in areas where removal is difficult (e.g., hair-bearing areas such as the eyebrow), or in patients who will not tolerate removal (e.g., children) or not return for suture removal. Nonabsorbable sutures are typically used in reliable patients and in areas under high tension (e.g., over a joint) or in areas of high cosmetic importance (e.g., face), where inflammation must be minimized to reduce scarring (with the exception of silk). Absorption of synthetic suture material occurs by hydrolysis and causes less tissue reaction than absorption of natural suture material, which occurs by proteolysis. Common rules for closure are that deep tissues should be approximated with 3-0 absorbable sutures and skin should be approximated with 4-0 to 6-0 suture depending on the location [*see Table 3*]. Areas of cosmetic importance (e.g., the face) should be approximated with 5-0 or 6-0 nonabsorbable suture, except in specific patients, as detailed above.

Staple closure is less expensive and significantly faster than suture closure and offers a slightly more acceptable cosmetic outcome when used to close scalp wounds.[30,31] Scalp wounds that are bleeding significantly can be quickly closed with staples to achieve hemostasis while the patient undergoes further evaluation and be revised later if needed. Contaminated wounds closed with staples have a lower incidence of infection than those closed with sutures due to their low level of tissue reactivity, but closure with staples is not a substitute for adequate wound irrigation and débridement.[32] In addition, staple closure eliminates the risk that a health care provider will experience a needle stick, which is a particularly important consideration in caring for a trauma patient with an unknown medical history. Staples are not suitable for wounds with irregular skin edges.

Tapes used for wound closure are either rubber based or employ an acrylate adhesive. Rubber-based tapes (e.g., athletic tape) are a potential irritant to skin; degrade with exposure to heat, light, and air; and are occlusive, thereby preventing transepidermal water loss. Tapes that include acrylate adhesives (e.g., Micropore and Steri-Strip), on the other hand, are hypoallergenic, have a long shelf life, and are porous, thereby allowing water to evaporate.[33] Linear wounds in areas with little tension with even wound edges are easily approximated with tape alone, whereas wounds in areas where the skin is more taut (e.g., the extremities) or uneven generally require that tape skin closure be supplemented by dermal sutures. The use of tape alone is desirable when feasible, especially in children, because it avoids the discomfort associated with suture placement and removal and prevents suture puncture scars.[33] However, tape is not a substitute for multilayered or meticulous wound closure. Tape closure has some other advantages: it may permit earlier suture removal; is easy to perform and comfortable for the patient; leaves no marks on the skin; and yields a lower infection rate in contaminated wounds than suture closure.[34] It also has a few disadvantages: patients may inadvertently remove the tape; wound edge approximation is less precise; tape will not adhere to mobile areas under tension (e.g., the plantar aspects of the feet) or to moist areas (e.g., mucous membranes and groin creases); wound edema can lead to blistering at the tape margins and to inversion of wound edges; and tape may elicit allergic reactions.

The use of tissue adhesives (e.g., octylcyanoacrylate) is a fast, strong, and flexible method of approximating wound

Table 3 Suggested Materials for Wound Approximation Based on Location

Location	*Suggested Closure Material*	*Suggested Time to Removal/Comments*
Deep structures (i.e., fascia, dermis, muscle)	3-0 or 4-0 absorbable suture depending on location	N/A
Oral/buccal mucosa	4-0 chromic gut	N/A
Lip	4-0 plain gut for wet vermillion 6-0 monofilament nonabsorbable for dry vermillion	5 days Ensure proper alignment of "red line" and "white line" of lip
Face	5-0 to 6-0 nonabsorbable monofilament 5-0 to 6-0 fast gut (children)	5 days
Ear	5-0 synthetic absorbable for cartilage 6-0 monofilament nonabsorbable for skin	5–7 days Bolster dressing to prevent hematoma or seroma formation
Scalp	3-0 monofilament nonabsorbable or absorbable suture Staples	10–14 days If injured, the galea must also be approximated with nonabsorbable suture
Other areas	3-0 absorbable or nonabsorbable Staples	7–10 days

N/A = not available.

edges. Compared with sutures, staples, and tapes, adhesives provide a faster closure and are essentially equivalent in terms of cosmetic outcome, infection rate, and dehiscence rate.[35] Adhesives can be used on most parts of the body and have been employed to close wounds ranging from 0.5 to 50 cm in length. Their advantages include reduced cost, ease of application, and the absence of any need for needles or suture removal. Their major disadvantage is lack of strength.[36] They must not be applied to tissues within wounds but rather should be applied to intact skin at wound edges where they hold injured surfaces together. In addition, they should not be used for wounds in mucous membranes, contaminated wounds, deep wounds, or wounds under tension. Adhesives are particularly useful for superficial wounds or wounds in which the deep dermis has been closed with sutures.

TIMING AND METHODS

After selecting the appropriate closure material, the timing of wound closure should then be addressed. The choices are (1) to close the wound at the time of initial presentation (primary intention), (2) to allow the wound to heal on its own (secondary intention), and (3) to delay closure until after a period of healing or wound care (tertiary intention). The best choice in a given situation depends on whether the patient is able to undergo wound repair, whether hemorrhage is under control, whether necrotic material has been adequately débrided and foreign bodies removed, the degree of bacterial contamination, the time since injury, and what the expected aesthetic outcome of immediate closure might be in comparison with delayed closure or healing by secondary intention.

The timing of wound closure and characteristics of the wound influence the method that will be chosen. The concept of the reconstructive ladder is commonly used to guide surgeons. In order of complexity, the closure methods available include (1) secondary closure; (2) primary closure; (3) delayed primary closure; (4) skin graft; (5) local flaps; (6) regional flaps (i.e., pedicled); (7) tissue expansion; and (8) free flaps. The ideal wound closure method supports the wound until it has reached near full strength (i.e., about 6 weeks), minimizes inflammation and ischemia, does not penetrate the epidermis and predispose to additional scars, and does not interfere with the healing process. Unfortunately, no existing method accomplishes all of these goals, and balancing them is virtually always necessary. Newer paradigms have also recognized the use of negative pressure wound therapy (NPWT) in place of skin grafts and dermal matrices in place of local flaps.[37]

Primary closure provides optimal wound healing when well-vascularized wound edges are approximated without tension. Closure should proceed from deep to superficial. The initial step is to identify landmarks and line up tissues using skin hooks or fine forceps to gently manipulate the tissue edges. Although wound approximation is usually a straightforward process, situations do arise where extra caution is necessary. For instance, when a wound crosses tissues with different characteristics (e.g., at the vermilion border of the lip, the eyebrow, or the hairline of the scalp), particular care must be taken to align the damaged structures accurately. In the repair of soft tissue, it is critical to handle tissue gently with atraumatic surgical technique, to place sutures precisely, and to minimize tension and contamination. If a wound is to be treated by primary intention, the wound edges should ideally be reapproximated by 6 to 8 hours, which is based on studies that examined the doubling time of bacterial colonization to an invasive infection.[11] Exceptions to this rule are acute wounds to the face, which may be closed up to 24 hours after injury due to the high vascularity of the face and importance of cosmesis.[38]

The next step is tissue-specific repair, which may require the consultation of an experienced surgeon. Bone fractures are reduced and repaired with plates, rods, or external fixation devices. Muscle lacerations should be repaired because muscle is capable of recovering a significant degree of strength. A completely lacerated muscle that is properly repaired recovers approximately 50% of its ability to produce tension and 80% of its ability to shorten, whereas a partially lacerated muscle that is properly repaired recovers approximately 60% of its ability to produce tension and 100% of its ability to shorten.[39] Tendon lacerations should be meticulously approximated to allow gliding and restore tensile strength. Either 4-0 multifilament polyester or monofilament polypropylene is a reasonable choice for muscle and tendon repair.[40] Early active mobilization promotes the restoration of tensile strength in muscles and tendons. Nerve trauma is treated with tension-free coaptation at the time of wound closure by primary repair or repair with a nerve graft or nerve tube. Epineurial coaptation is typically achieved by placing 8-0 to 10-0 monofilament nylon sutures under loupe or microscope magnification. For ischemic or amputated tissues (e.g., an ear, a digit, or a limb), vessel repair is performed with 8-0 to 10-0 monofilament nylon sutures under magnification.

Suture placement in subcutaneous fat should be avoided whenever possible. If sutures in this location are absolutely necessary, they should be placed at the fat-fascia junction or the fat-dermis junction and not in fat alone. Fat cannot hold sutures by itself, and because it has a poor blood supply, suturing may lead to fat necrosis and increased risk of infection.[29] The deeper fascial layers that contribute to the structural integrity of areas such as the abdomen, the chest, and the galea should be closed as a separate layer to prevent hernias, structural deformities, and hematomas.

At the skin level, the deep dermis is responsible for the strength of the acute wound closure. Deep dermal repair is performed with absorbable suture material (e.g., polyglactin [910]). The size of the suture is based on the anatomic location of the wound and the age of the patient [*see Table 3*]. Sutures are buried and placed 5 to 8 mm apart, with care taken to evert the skin edges. Buried dermal sutures are often used in conjunction with tapes (e.g., Steri-Strips), fine epidermal sutures, or adhesives to facilitate precise alignment. Skin edges should be coapted and everted with 4-0 to 6-0 nylon or polypropylene sutures placed in the superficial dermis and the epidermis. The distance between the sutures and the distance between the wound edge and the suture insertion point should be equal to the thickness of the skin (epidermis and dermis combined).

Several different skin suturing methods may be used depending on the nature of the wound. Simple interrupted sutures are useful for irregular wounds. Vertical mattress

sutures are good for either thick (e.g., scalp) or thin (e.g., eyelid) skin. Horizontal mattress sutures can lead to ischemia and must not be applied too tightly. They may look untidy early after repair, but, generally, good wound-edge eversion and long-term healing are achieved. Half-buried horizontal and vertical mattress sutures are used for flap edges to minimize ischemia. A continuous intradermal or subcuticular suture is easy to remove and best suited for epidermal tissue approximation. It may only be used on tension-free wound closures and thus is often used in conjunction with other closure techniques (i.e., deep dermal stitches). A simple continuous skin suture should be used only for linear wounds. Although it is quick to place, it tends to invert the wound edges. Flap tips should be sutured with a three-point method to prevent strangulation [*see Figure 1*]. For children, suture removal can be both emotionally and physically traumatic; accordingly, when suturing is employed for skin closure in a pediatric patient, the use of fast-absorbing suture material (e.g., plain catgut) or a pullout continuous subcuticular suturing method should be considered. Alternatively, dermal closure may be used in conjunction with adhesives in children, patients who will not follow up, or individuals who are prone to keloid formation.[29]

Secondary intention, in which the wound is left open and allowed to heal on its own, is sometimes chosen. Secondary closure depends on contraction of the surrounding tissue and epithelialization from the wound margins. With this approach, caution and close observation are essential because the process of tissue contraction can sometimes lead to contracture. Secondary closure can, however, yield acceptable results with specific wound types and at specific anatomic sites. With puncture wounds, for example, secondary closure is preferred because it diminishes the likelihood of infection. For both abrasions and puncture wounds, the functional and aesthetic results of secondary closure are generally as good as or better than those obtained by primary or delayed primary closure. For wounds on anatomically concave surfaces (e.g., the medial canthal region, the nasolabial region, or the perineum), secondary wound healing also generally yields excellent results.[41] Secondary closure should additionally be considered for severely contaminated wounds, infected wounds, wounds with significant amounts of devitalized tissue, wounds with foreign bodies, lacerations older than 24 hours, wounds in patients who are in shock, and high-velocity wounds.[42]

Delayed primary closure is performed in cases where obvious bacterial contamination is present, there is a substantial amount of necrotic tissue, or the patient is unstable and unfit to undergo primary repair. Delayed primary closure involves direct approximation of wound edges after a period (usually 4 to 5 days) of wound care and has been shown to diminish the incidence of wound infection in contaminated wounds. Quantitative microbiology can help guide the decision to perform delayed closure because bacterial counts less than 10^5 are unlikely to become infected.[41–43] Except for dressing changes (typically two to four times per day depending on the amount of drainage), these wounds should not be disturbed for the first 4 days after initial irrigation and débridement unless fever develops. However, heavily contaminated wounds may benefit from repeat washout 24 hours after the initial débridement or the use of NPWT or both [*see* Dressings for Specific Types of Wounds, *below*] to handle large amounts of exudate. Fasciotomy closure is an excellent example of when delayed primary closure is beneficial. Following a fasciotomy, the swollen extremity is unsuitable for closure. However, after a period of local wound care where time is given for the edema to subside, the skin edges are approximated to accelerate healing and reduce scar formation.

Occasionally, an acute wound is so large that neither primary nor secondary closure will suffice. Such wounds must be covered with skin grafts or transferred tissue (i.e., flaps). Local, regional, or free flaps must be considered for wounds that involve exposed bone denuded of periosteum, cartilage denuded of perichondrium, tendon denuded of paratenon, or nerve denuded of perineurium.

Adjunctive Wound Treatment

PROPHYLACTIC SYSTEMIC ANTIBIOTICS

For most wounds, antibiotic prophylaxis is not indicated as the endogenous flora is less than 10^3 and usually not a source of infection.[17] Estimates of traumatic wound infection

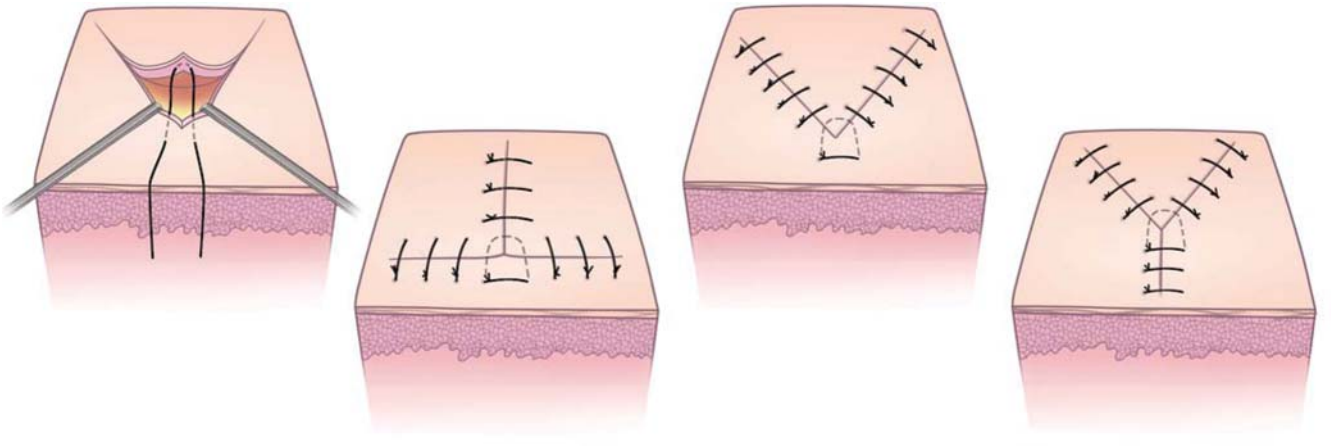

Figure 1 **The method for inserting three-point sutures, along with three different applications of this method.**

vary from 4.5 to 6.3%,[38] and a meta-analysis of randomized trials does not support the use of antibiotics in simple wounds.[44] When antibiotics are called for, the agent or agents should be selected on the basis of the bacterial species believed to be present. The anatomic location of a wound may also suggest whether oral flora, fecal flora, or some less aggressive bacterial contaminant is likely to be present. Gram staining can provide an early clue to the nature of the contamination. Ultimately, the choice of a prophylactic antibiotic regimen is based on the clinician's best judgment regarding which agent or combination of agents will cover the pathogens likely to be present and the patient's risk factors (e.g., recent hospitalization, methicillin-resistant *Staphylococcus aureus* [MRSA] exposure). Antibiotics should be administered immediately when indicated because as time progresses, fibrinous coagulum from the surrounding wound surrounds and protects the bacteria.[17] Oral antibiotics appear to be as effective as parenteral antibiotics for wound infection prophylaxis except in the case of open fractures.[45] When antibiotics are used for prophylaxis against wound infection, they should be continued only for 24 hours or until definitive closure is performed. Wound infections will typically occur at 4 to 5 days after injury unless group A *Streptococcus* or *Clostridium* is the causative agent, both of which may cause infection within 24 hours.

The American College of Surgeons (ACS) has divided wounds into four major categories: clean, clean-contaminated, contaminated, and dirty [*see Table 4*]. The likelihood of infection after any surgical procedure is correlated with the ACS wound category: class I and II wounds have infection rates lower than 11%, whereas wounds in class IV have infection rates as high as 40%.[46]

As a rule, clean and clean-contaminated wounds are adequately treated with irrigation and débridement. There are, however, some local factors (e.g., impaired circulation and radiation injury) and systemic factors (e.g., diabetes, AIDS, uremia, and cancer) that increase the risk of wound infection. In the presence of any of these factors, prophylactic antibiotics should be considered. In addition, prophylactic antibiotics should be given to patients with extensive injuries to the central area of the face (to prevent spread of infection through the venous system to the meninges), patients with valvular disease (to prevent endocarditis), and patients with prostheses (to reduce the risk of bacterial seeding of the prosthesis). Lymphedematous extremities are especially prone to cellulitis, and antibiotics are indicated whenever such extremities are wounded. Antibiotics are also indicated in the treatment of open fractures, typically with a first-generation cephalosporin that should be administered within 6 hours following injury and up to 24 hours after wound closure. If gross contamination or extensive soft tissue damage is present, an aminoglycoside is added and antibiotics are continued for 72 hours or 24 hours after wound closure.[38,47]

Contaminated and dirty wounds are associated with a higher risk of infection and are therefore more likely to necessitate antibiotic prophylaxis. Human bite wounds, mammalian bite wounds, and wounds contaminated with dirt, bodily fluids, or feces are all prone to infection and must be treated with antibiotics.[48,49] Prophylactic administration of a combination of a β-lactam antibiotic with a β-lactamase inhibitor (e.g., amoxicillin-clavulanate) is appropriate.[45,50] Antibiotic prophylaxis is also indicated for mutilating wounds with extensive amounts of devitalized tissue. Such wounds are often contaminated by a mixture of gram-positive organisms and gram-negative organisms.[51] When antibiotics are indicated for these injuries, broad-spectrum coverage is appropriate, typically for 3 to 5 days[38]

TOPICAL ANTIMICROBIALS

Wounds contaminated by bacteria can be treated with dressings that contain antibacterial agents such as mafenide, silver nitrate, silver sulfadiazine, or iodine. These agents may help reduce bacterial load and the rate of infection but may also cause significant side effects. For instance, mafenide penetrates eschar well but can cause pain and has the potential to induce metabolic acidosis through inhibition of carbonic anhydrase. Silver nitrate does not cause pain but can cause hypochloremia, and it stains fingernails and toenails black. Silver sulfadiazine, which is most commonly used for burn care due to its ability to maintain a moist wound environment (thereby speeding healing and epithelialization), has been associated with transient leukopenia.[52] Ultimately, the choice of topical agent is based on the type of wound, the degree of contamination, the potential for infection, the likely offending organism, and the clinician's judgment.

Although topical antimicrobials (e.g., antibiotic ointments, iodine preparations, and silver agents) are commonly used to prevent wound infection, their benefit is unclear. For instance, whereas application of bacitracin and neomycin ointment results in a significantly lower infection rate than application of petrolatum in uncomplicated traumatic wounds,[53] similar application of mupirocin ointment to a

Table 4 Classification and Infection Rates of Operative Wounds[46]

Classification	*Infection Rate (%)*	*Wound Characteristics*
Clean (class I)	1.5–5.1	Atraumatic, uninfected; no entry of GU, GI, or respiratory tract
Clean-contaminated (class II)	7.7–10.8	Urgent or emergency case that is otherwise clean; minor breaks in sterile technique; entry of GU, GI, or respiratory tract without significant spillage
Contaminated (class III)	15.2–16.3	Traumatic wounds; gross spillage from GI tract; entry into infected tissue, bone, urine, or bile; penetrating trauma < 4 hours old
Dirty (class IV)	28.0–40.0	Drainage of abscess; débridement of soft tissue infection; penetrating trauma > 4 hours old

GI = gastrointestinal; GU = genitourinary.

clean surgical wound did not reduce the infection rate and actually promoted antibiotic resistance.[54] Additionally, whereas neomycin-containing ointments reduce bacterial counts in partial-thickness wounds in animals, many other over-the-counter antibiotic ointments were not effective in reducing bacterial counts.[55] In general, topical antimicrobials seem best suited for burns and open, grossly contaminated wounds. They seem to have no role after definitive closure is performed except when used in place of a dressing.

TETANUS PROPHYLAXIS

Tetanus is a nervous system disorder that is caused by *Clostridium tetani* and is characterized by muscle spasm. In the past, wounds were classified as either tetanus prone or non–tetanus prone on the basis of their severity. However, it has been demonstrated that wound severity is not directly correlated with tetanus susceptibility and that tetanus has been associated with a wide variety of injury types over a broad spectrum of wound severity.[56] Accordingly, all wounds, regardless of cause or severity, must be considered tetanus prone, and the patient's tetanus immunization status must always be considered. Tetanus wound prophylaxis should be provided as appropriate [*see Table 5*].[56,57]

RABIES PROPHYLAXIS

Rabies is an acute and progressive encephalitis that is caused by viruses from the family Rhabdoviridae. The rabies virus can be transmitted by any mammal, but viral reservoirs are found only in carnivores and bats. In North America, raccoons, skunks, bats, and foxes are the animals most commonly responsible for transmission.[58] Bite wounds in which the animal's saliva penetrates the dermis are the most common cause of exposure.

Post exposure treatment consists of wound care, infiltration of rabies immune globulin into the wound (passive immunity), and administration of vaccine (active immunity).[58,59] Wound care involves washing with soap and water as well as the use of iodine- or alcohol-based virucidal agents.[60] Guidelines for postexposure prophylaxis have been established [*see Table 6*]. The vaccination regimen is determined by the patient's previous vaccination status [*see Table 7*].

Table 5 Recommendations for Tetanus Immunization[56,57,208]

Tetanus Immunization History	*Clean and Minor Wounds*		*All Other Wounds*†	
	*Td**	*TIG*	*Td*	*TIG*
< 3 doses or unknown	Yes	No	Yes	Yes
≥ 3 doses	Only if last dose given ≥ 10 years ago	No	Only if last dose given ≥ 5 years ago	No

Tetanus-diptheria (Td) vaccine and tetanus immune globulin (TIG) should be administered with separate syringes at different anatomic sites. Tetanus and diphtheria toxoids are contraindicated for the wounded patient if there is a history of a neurologic or severe hypersensitivity reaction after a previous dose. Local side effects alone do not preclude continued use. If a systemic reaction is suspected of representing allergic hypersensitivity, immunization should be postponed until appropriate skin testing is performed. If a contraindication to a Td-containing preparation exists, TIG alone should be used.
*For patients younger than 7 years, tetanus-diphtheria-acellular pertussis vaccine (Tdap) (or tetanus and diphtheria toxoids if pertussis vaccine is contraindicated) is preferable to Td alone. For patients 7 years of age or older, Td alone may be given.
†Wounds contaminated with dirt, feces, soil, or saliva; puncture wound; avulsions; wounds from missiles, crushing wounds, burns, or frostbite.

Closure of Specific Types of Wounds

Wounds may be divided into 10 main types: abrasions, lacerations, puncture/penetrating, complex, crush injuries, extravasation injuries, injection injuries, high velocity, bites, and stings. Antibiotic recommendations for different injuries are summarized below [*see Table 8*].

ABRASIONS

Abrasions are superficial wounds caused by scraping. They involve only the epidermis and a portion of the dermis and frequently heal secondarily within 1 to 2 weeks. If an abrasion is to be closed primarily, tape or glue may be used for epidermal approximation to prevent suture mark scars, which could be worse than the actual wound scar. In some patients who have experienced abrasion injuries (e.g., motorcycle accidents in which victims slide along asphalt) or blast injuries (e.g., firework explosions), small foreign body fragments become embedded in and beneath the skin. Complete débridement of these embedded foreign bodies within 24 to 48 hours of injury is crucial to preventing traumatic tattooing. In the early post injury period, surgical débridement with a small drill, a sharp instrument, or a preoperative hand surgical scrub brush may suffice for removal of the foreign material. It traumatic tattooing still occurs, dermabrasion may be necessary.[61,62] Once the wound is adequately débrided, semiocclusive dressings should be applied to optimize epithelialization. Antibiotics are rarely indicated for these types of injuries.

LACERATIONS

The type of wound most commonly encountered by surgeons is a superficial or deep acute traumatic wound that is suitable for primary closure. In this setting, the goal is to provide the best possible chance for uncomplicated healing. As a rule, closure should be completed within 6 to 8 hours of the injury, although simple noncontaminated wounds of the face can be safely closed up to 24 hours after the injury.[38] Primary closure eliminates the need for extensive wound care, allows the wound to heal more quickly, minimizes patient discomfort (i.e., dressing changes), and has a superior cosmetic outcome. However, lacerations containing foreign bodies or necrotic tissue that cannot be removed by irrigation or débridement and lacerations with excessive bacterial contamination should not be closed primarily, nor should wounds in which hemostasis is incomplete. Hematomas, necrotic tissue, and foreign bodies all promote bacterial growth and place a mechanical barrier between healing tissues.[63–65] Only contaminated wounds or wounds in high-risk patients (i.e., diabetes, cancer) should be considered for prophylactic antibiotics.

Table 6 Recommendations for Postexposure Rabies Prophylaxis

Animal Type[58–60,209]	*Animal Disposition and Evaluation*	*Prophylaxis*
Dogs, cats, ferrets	If animal is healthy and available, it is confined for 10 days of observation	Start vaccination if animal exhibits rabies symptoms*
	If animal is rabid or suspected of being rabid, no observation is indicated	Provide immediate vaccination
	If animal's rabies status is unknown, consultation is indicated	Consult public health official
Bats, skunks, raccoons, foxes, bobcats, coyotes, mongooses, and most carnivores	Animal is regarded as rabid unless brain laboratory tests are negative	Provide immediate vaccination unless brain laboratory tests are negative
Livestock, small rodents (e.g., squirrels, chipmunks, rats, hamsters, gerbils, guinea pigs, and mice), large rodents (e.g., woodchucks and beavers), rabbits, hares, and other mammals	Each case is considered individually; rabies reported in large rodents in some areas	Consult public health officials; almost never require rabies treatment

*If the isolated animal shows symptoms of rabies, postexposure prophylaxis is started immediately, and the animal is euthanized for laboratory testing. Vaccination prophylaxis is stopped if laboratory tests are negative for rabies.

Table 7 Recommendations for Postexposure Rabies Vaccination[58–60,209]

	Dosage	
	No Previous Vaccination	*Previous Vaccination*
Human rabies immune globulin (HRIG)	Full dose of 20 IU/kg infiltrated around wound(s) at initial presentation; use separate syringe and anatomic site from vaccine	Not administered
Human diploid cell vaccine (HDCV), rabies vaccine absorbed (RVA), or purified chick embryo cell vaccine (PCECV)	1.0 mL IM on days 0, 3, 7, 14*	1.0 mL IM on days 0 and 3*

IM = intramuscularly.
*Vaccine administration site for adults is the deltoid; for children, the anterolateral thigh may be used. To prevent sciatic nerve injury and reduce adipose depot delivery, the gluteus is never used.

Table 8 Antibiotic Recommendations for Common Injuries[38,45,50,80]

Injury	*Pathogen*	*Treatment*	*Notes*
Cat bite/ dog bite	*Pasteurella multocida* (cats) *Pasteurella canis* (dogs) *Staphylococcus* species, *Streptococcus* species, *Pseudomonas* species *Anaerobes*	Amoxicillin-clavulanate	Must thoroughly washout and débride Rule out joint involvement Dog bites carry less risk of infection than cat or human bites Consider use of parenteral antibiotics in patients with evidence of infection Doxycycline with metronidazole or clindamycin is good alternative if the patient has known penicillin allergy Treatment for uncomplicated cases is typically 3–5 days
Fracture (open)	*Staphylococcus aureus* *Streptococcus* Gram negatives	First-generation cephalosporin ± aminoglycoside (gentamicin)	Add aminoglycoside if gross contamination or extensive soft tissue injury Must thoroughly wash out and débride Treatment course typically 24 hours If gross contamination, antibiotics continued for 72 hours or up to 24 hours after wound closure
Human bite	*Streptococcus viridans* *S. aureus* *Eikenella corrodens* Anaerobes	Amoxicillin-clavulanate	Ciprofloxacin with clindamycin is good alternative if the patient has known penicillin allergy Treatment typically 3–5 days
Soft tissue trauma	Group A *Streptococcus* *S. aureus*	First-generation cephalosporin or antistaphyloccal penicillin (i.e., nafcillin or oxacillin)	Only indicated when high-risk factors present (i.e., contamination, penetrating wounds, systemic disease such as diabetes, cancer) If used, discontinue after definitive closure (typically within 24 hours) Clindamycin is a good alternative if the patient has known penicillin or cephalosporin allergy. Add *Pseudomonas* coverage for farming and industrial accidents Consider MRSA coverage in patients with prior history or high risk patients (i.e., incarcerated or hospitalized) Consider adding a penicillin and Peridex oral rinse (chlorhexidine gluconate) for intraoral trauma

MRSA = methicillin-resistant *Staphylococcus aureus*.

PUNCTURE/PENETRAING WOUNDS

Puncture wounds should be examined for foreign bodies and removed. These are typically left open, treated with wound care, and allowed to heal by secondary intention. With puncture wounds, secondary closure reduces the risk of infection and generally yields excellent aesthetic results. All puncture wounds should raise suspicion for underlying nerve, muscle, tendon, vessel, and organ injury. Almost all penetrating abdominal and chest injuries should be considered for operative exploration. Penetrating wounds of the abdomen also should receive antibiotics to lower the rate of postoperative peritonitis with a single-agent regimen using a β-lactam antibiotic with aerobic gram-negative and anaerobic activity for 24 hours.[38]

COMPLEX WOUNDS

The term *complex wound* includes stellate wounds, degloving, avulsion, open fractures, and mutilation injuries. The goals of treatment include achieving closure within 6 to 8 hours of the injury, providing treatment in a manner consistent with the patient's general health, protecting tissues from desiccation, and supplying adequate permanent coverage. Antibiotics should be considered for these types of injuries. In addition, it is important to discuss with the patient the particular treatment difficulties posed by these wounds. Often a patient with a complex wound must be treated in the operating room under general anesthesia to adequately explore the tissues, remove foreign bodies, and débride nonviable tissue.

Stellate wounds can be approximated with careful placement of interrupted and three-point sutures. Severely injured tissue may have to be removed as an ellipse with the resulting defect closed primarily.

Degloving refers to circumferential elevation of skin and fat from muscle. Given that the skin flap blood supply is primarily provided by the dermal plexus, it rarely survives in this type of injury. Therefore, in the acute setting, questionably viable flaps of tissue may be evaluated by administering fluorescein, up to 15 mg/kg IV, and observing the flap for fluorescence under an ultraviolet lamp after 10 to 15 minutes.[66] Viable flap tissue fluoresces green. Tissue that is devascularized should be débrided. If the viability of a tissue segment is in doubt, the segment may be sewn back into its anatomic location and allowed to define itself over time.

Large open wounds resulting from avulsion can be either left to heal by secondary intention or treated with delayed skin grafting.[42]

Open fractures are at high risk for development of osteomyelitis, and a high suspicion should be maintained when any break in the skin is present over a known fracture. These wounds should be thoroughly explored, with removal of any debris and copious irrigation. Urgent orthopedic consultation is needed for operative débridement, and antibiotics are indicated.[38]

Mutilating wounds caused by machinery (e.g., farm equipment) are often contaminated by a mixture of gram-positive and gram-negative organisms, although not always excessively.[51] When such a wound is grossly contaminated, antibiotic therapy (preferably with an agent or combination of agents that offers broad-spectrum coverage) is indicated. Contaminated wounds closed with either tape or staples have a lower incidence of infection than those closed with sutures.[32,34]

CRUSH INJURIES

A notable feature of crush injury is that the severity of the wound is not always readily apparent. In some cases, no external laceration can be seen, even though deep tissue damage may be extensive. For this reason, antibiotics are generally recommended.[38] Ultrasonography or magnetic resonance imaging may help identify a hematoma that is amenable to evacuation.[42] Deep tissue injury can lead to compartment syndrome and subsequent extremity loss. Early diagnosis is the key to successful treatment. Generally, the diagnosis can be made on the basis of physical signs and symptoms (the six Ps), including increasing pain that is out of proportion to the stimulus, diminished sensation (paresthesias), muscle weakness (paresis), relative cooling of the skin (poikilothermia), pallor, and pulselessness. It should be emphasized that loss of pulses is often a late finding of compartment syndrome, and distal pulses do not exclude the diagnosis. Other important signs include pain on passive stretching of the affected muscle compartment and palpable tenseness of the compartment.[67] Although the sensitivity and positive predictive value for clinical findings are low, the specificity and negative predictive value are greater than 95%. The probability of compartment syndrome with any three of pain, paresthesia, pain with passive stretch, and paresis is approximately 93%.[68]

If compartment syndrome is suspected, appropriate therapeutic measures should be taken, including restoration of normal blood pressure in the hypotensive patient, removal of all constrictive dressings, and maintenance of the limb at the heart level.[1] Although compartment syndrome is a clinical diagnosis, measurements of intracompartmental pressure may aid in the diagnosis.[69] If the delta pressure (i.e., the diastolic blood pressure minus the intracompartmental pressure) is less than or equal to 30 mm Hg, compartment syndrome is considered to be present. Once diagnosed by an abnormal delta pressure and/or persistent clinical symptoms and signs despite conservative measures, fasciotomies should be performed as soon as possible and within 6 hours.[67,69] Compartment syndrome with muscle damage can also lead to rhabdomyolysis and renal failure. If an elevated serum creatinine kinase concentration is reported, intravascular volume is stabilized, and urine flow is confirmed, a forced mannitol-alkaline diuresis may be beneficial as prophylaxis against hyperkalemia and acute renal failure.[70]

EXTRAVASATION INJURIES

In patients with arterial or venous catheters, a vessel may become occluded or a catheter dislodged from the intravascular space. When this occurs, solutions or medicines are delivered into the interstitial space and may cause extravasation injury. Most acute extravasation injuries are quickly diagnosed and heal without complications with conservative management (i.e., stopping the infusion, removal of the catheter, elevation of the limb, application of ice packs, and careful monitoring).[71] However, extravasation injuries

involving high fluid volumes, high-osmolar contrast agents, or chemotherapeutic drugs can have more serious effects, such as skin ulceration and extensive soft tissue necrosis similar to a chemical burn. Treatment of these injuries is not standardized. It may include conservative management, hydrocortisone cream, incision and drainage, hyaluronidase injection, saline injection, and aspiration by means of liposuction.[71–73]

INJECTION INJURIES

Wounds caused by injection of foreign materials (e.g., paint, oil, grease, or dirty water) can be severe. Injection injuries usually result from the use of high-pressure spray guns (600 to 12,000 psi) and often occur on the nondominant hand.[74,75] On the initial examination, the injury may appear deceptively benign, with only a punctate entry wound visible; however, foreign material is often widely distributed in the deeper soft tissues. Radiographs are obtained to identify any fractures present and, in some cases, to determine the extent to which the injected material is distributed. Injection wounds must be treated aggressively with incision, wide exposure, débridement, and removal of foreign bodies to prevent extensive tissue loss and functional impairment. The functional outcome is determined by the time elapsed between injury and treatment and by the type of material injected. Oil-based paint is more damaging to tissues than water-based paint, oil, grease, water, or air.[76,77]

PROJECTILE WOUNDS

Projectile injuries are divided into low- and high-velocity wounds. Low velocity is defined as speeds up to 350 m/s, whereas high-velocity projectiles travel over 600 m/s. The distinction has clinical importance because with low-velocity projectiles, tissue damage is confined to the bullet tract. On the other hand, high-velocity wounds from explosions or gunshots cause extensive tissue damage due to the release of significant kinetic energy.[17] Small entry wounds are common, but the seemingly benign appearance of such a wound often belies the actual severity. As the bullet travels through the soft tissue, it does not follow a linear path but rather tumbles. Thus, the exit wound and interspace may contain large areas of ischemic and damaged tissue that affect critical structures (e.g., bone and blood vessels). Clothing and dirt may also be transmitted into the deep spaces. Radiographs may identify radiopaque foreign bodies (e.g., metal objects or pieces of leaded glass).[78] Treatment of wounds created by high-velocity missiles involves extensive débridement and identification of injured tissue. Wounds should be left open to heal by secondary or delayed primary closure.[42] Antibiotics are indicated to prevent bacteremia[17] except in soft tissue–only gunshot wounds.[79]

BITE WOUNDS

Treatment of bite wounds involves thorough exploration, irrigation, and débridement. X-rays must be obtained and wounds explored to evaluate the patient for fractures or open joint injuries. If a joint capsule has been violated, the joint must be thoroughly cleaned. Due to the infection risk, wounds may be allowed to heal by secondary intention or delayed primary closure. Primary closure is also possible if thorough débridement is performed,[42] but no prospective data exist, and this area remains highly controversial. Facial wounds may be considered for closure given the area's cosmetic importance and overall lower risk of infection. Delayed primary closure with a 3- to 5-day interval may also be considered as this may give a better cosmetic result than healing by secondary intention. Irrigation is the most important factor in decreasing the bacterial load.[38] Rabies prophylaxis treatment should be considered for patients who have been bitten by wild animals [*see* Adjunctive Wound Treatment, Rabies Prophylaxis, *above*].

Humans and Nonvenomous Animals

Most human bite wounds are clenched-fist wounds sustained by young men.[80] Human bite wounds are considered infected from the moment of infliction and must be treated with antibiotics.[48,49] The antibiotic regimen should be targeted against the bacterial species most likely to be present. Common isolates from bite wounds include *Streptococcus anginosus*, *Staphylococcus aureus*, *Eikenella corrodens*, *Fusobacterium nucleatum*, *Prevotella melaninogenica*, and *Candida* species.[80] To cover these organisms, a broad-spectrum antibiotic or combination of antibiotics (e.g., amoxicillin-clavulanate or moxifloxacin or ciprofloxacin with clindamycin in patients with a penicillin allergy) should be administered.[80] Infections related to human and animal bites develop within 12 to 24 hours of the injury.[38]

Nonhuman primates can cause viral infection, most commonly with cercopithecine herpesvirus type 1. If left untreated, such infection can lead to meningoencephalitis, which carries a 70% mortality. Accordingly, acyclovir prophylaxis is recommended.[81]

Wounds caused by cat bites or scratches are at high (80%) risk for infection that is usually attributable to *Pasteurella multocida*. The aerobic species commonly isolated from such wounds include *Pasteurella*, *Streptococcus*, *Staphylococcus*, *Moraxella*, and *Neisseria*; common anaerobic isolates include *Fusobacterium*, *Bacteroides*, *Porphyromonas*, and *Prevotella*.[50] Patients with severe infection should be treated with parenteral antibiotics (i.e., ampicillin-sulbactam). Acute regional lymphadenitis after a cat scratch is known as cat-scratch disease and is caused by *Bartonella henselae*.[82] It is treated by administering azithromycin.[83] Cat bites should not be closed.

Dog bite wounds are at lower (16%) risk for infection than human bite or cat bite wounds and tend to be less severely contaminated. The aerobic and anaerobic organisms commonly found in cat bite wounds are similar to those found in dog bite wounds, and antibiotic prophylaxis with a combination of a β-lactam antibiotic with a β-lactamase inhibitor (e.g., amoxicillin-clavulanate) is appropriate.[45,50]

Venomous Animals

Snake bites Four types of poisonous snakes are native to the United States. These include the coral snakes (*Micrurus* and *Micruroides* species) from the family Elapidae and three species of pit vipers from the family Viperidae: rattlesnakes (*Crotalus* species), copperheads (*Agkistrodon tortortrix*), and cottonmouths or water moccasins (*Agkistrodon piscivorus*).[84–86] Pit vipers can be identified by the pit between the eye and the nostril on each side of the head, the vertical elliptical pupils, the triangle-shaped head, the single row of

subcaudal plates distal to the anal plate, and the two hollow fangs protruding from the maxilla that produce the characteristic fang marks.[87] Coral snakes have rounder heads and eyes and lack fangs. They are identified by their characteristic color pattern consisting of red, yellow, and black vertical bands.

Patients bitten by coral snakes show no obvious local signs when envenomation has occurred. Consequently, the physician must look for systemic signs such as paresthesias, increased salivation, tongue fasciculations, dysphagia, dysarthria, visual disturbances, respiratory distress, convulsions, and shock. These symptoms may not develop until several hours after the bite. On the other hand, patients bitten by pit vipers typically develop local pain and swelling within 30 minutes of the bite. In some cases, these manifestations may take up to 4 hours to appear. Erythema, petechiae, bullae, and vesicles are also sometimes seen. Severe envenomation may induce systemic reactions, including disseminated intravascular coagulation (DIC), bleeding, hypotension, shock, acute respiratory distress syndrome (ARDS), and renal failure.

If signs or symptoms of envenomation are found, appropriate laboratory tests (hematocrit, fibrinogen level, coagulation studies, platelet count, urinalysis, and serum chemistries) should be ordered. Laboratory tests should be repeated every 8 to 24 hours for the first 1 to 3 days to determine whether envenomation is progressing. Severe envenomation can cause decreased fibrinogen levels, coagulopathy, bleeding, and myoglobinuria.

Treatment of venomous snake bites includes immobilization and elevation. If envenomation is suspected or confirmed, antivenin should be administered intravenously as early as possible. Antivenins commonly used in the United States include Antivenin (Crotalidae) Polyvalent (ACP) (Wyeth Pharmaceuticals, Collegeville, PA) and Crotalidae Polyvalent Immune Fab (Ovine) (CroFab, Protherics Inc., Nashville, TN).[88] Fab antivenom (FabAV) is less allergenic and more potent than ACP and thus has largely supplanted it in the United States.[88,89] Patients are treated with a loading dose of four to six vials of FabAV followed by three two-vial maintenance doses at 6, 12, and 18 hours to prevent recurrence of symptoms. If symptoms progress despite antivenin treatment, an additional four to six vials of FabAV are given twice more. If symptoms continue to progress, consideration should be given to using ACP. ACP remains the most effective antivenin for patients with coral snake bites and those who do not respond to FabAV. Before ACP is administered, the patient must be tested for sensitivity. The major complication of antivenin therapy is serum sickness. This complication occurs in approximately 50 to 75% of patients treated with ACP but in only 16% of those treated with FabAV.[88,90,91]

Compartment syndrome is a rare but severe complication of a snake bite. Fasciotomy is sometimes required to relieve extremity compartment syndrome, but it is not necessary for prophylactic purposes. Tourniquets, incision and suction, cryotherapy, and electric shock treatment are of little value for snake bites and may increase complication rates. There is no clear evidence to support antibiotic prophylaxis in this setting.[87]

Spider bites The bites of most spiders found in the United States cause little to no wound or local reaction; however, three types are capable of injecting venom. Brown recluse spiders (*Loxosceles reclusa*) can be identified by a violin-shaped dorsal mark. They are nocturnal, live in dark and dry places, and are found in the central and southern United States. The venom is a phospholipase enzyme that acts as a dermal toxin and almost always causes a local reaction.[92] Local signs and symptoms may be limited to minor irritation, although they may also progress to extreme tenderness, erythema, and edema. The onset of symptoms may be delayed for as long as 8 hours, and tissue necrosis may develop over the following days to weeks. Systemic reactions may include mild hemolysis, mild coagulopathy, and DIC, although severe intravascular hemolytic syndrome and death have also been reported.[92,93] Oral administration of dapsone (50 to 100 mg/day) to minimize tissue necrosis has been advocated by some[94]; however, this treatment is of uncertain efficacy, and no prospective data currently support its use. Moreover, dapsone can cause hemolytic anemia, a potentially life-threatening condition.[93] If systemic symptoms develop, systemic corticosteroid therapy and supportive measures are indicated. Brown recluse antivenin is not available in the United States.

Black widow spiders (*Latrodectus mactans*) can be identified by a red-hourglass ventral mark.[86] They live in dark, dry, and protected areas and are distributed widely throughout the continental United States. The venom is a neurotoxin that produces immediate and severe local pain. Local signs and symptoms include two fang marks, erythema, swelling, and piloerection.[92] Systemic reactions with neurologic signs may develop within 10 minutes and include muscle pain and cramps starting in the vicinity of the bite, abdominal pain, vomiting, tremors, increased salivation, paresthesias, hyperreflexia, and, with severe envenomation, shock. Systemic symptoms may last for days to weeks. High-risk persons (e.g., those who are younger than 16 years, the elderly, pregnant women, hypertensive patients, or persons who continue to show symptoms despite treatment) may experience paralysis, hemolysis, renal failure, or coma. Treatment includes 10% calcium gluconate IV for relief of muscle spasm, methocarbamol or diazepam for muscle relaxation, and a single dose of antivenin. Antivenin causes serum sickness in as many as 9% of patients; consequently, its use is controversial except in high-risk patients.[95]

Hobo spiders (*Tegenaria agrestis*) can be identified by their long hairy legs and a cephalothorax that is marked by two stripes and butterfly markings dorsally and two stripes ventrally. Found throughout the northwestern United States, they live in low places and build funnel-shaped webs in dark spaces. Hobo spiders have been reported to inflict painful bites that lead to wound ulceration, dermonecrosis, and a persistent headache, although the accuracy of such reports has been debated.[93,96,97] A slow-healing ulcer that leaves a central crater has been described. Treatment consists of local wound care.

Scorpions Stings from most scorpion species found in the United States cause only limited local reactions that

can be managed conservatively; however, stings from *Centruroides sculpturatus*, which is found in California and many southern states, may be more severe. *Centruroides* has a sting that causes envenomation with a neurotoxin. Erythema, edema, and ecchymosis at the site of the sting are evidence that envenomation did not take place. Instead, envenomation is indicated by an immediate and intense burning pain at the wound site.[98] The initial local pain may then be followed by systemic symptoms such as muscle spasm, excess salivation, fever, tachycardia, slurred speech, blurry vision, convulsions, or death.[92] Treatment consists of icing and elevation of the wounded area followed by administration of barbiturates for control of neuromuscular activity and institution of supportive therapy with antihistamines, corticosteroids, and analgesics.[98]

Centipedes Centipedes are slender, multisegmented, and multilegged arthropods that range in size from 1 to 30 cm and in color from bright yellow to brownish black. The first pair of legs is modified into sharp, stinging structures that are connected to venom glands. Centipedes prefer dark, damp environments and may be found throughout the southern United States. Local symptoms associated with centipede stings include pain, erythema, edema, lymphangitis, lymphadenitis, weakness, and paresthesia. Skin necrosis may occur at the envenomation site. Systemic symptoms may include anxiety, fever, dizziness, palpitations, and nausea.[99] Treatment consists of symptomatic pain control, infiltration of local anesthetics, administration of antihistamines, and local wound care.[99]

Hymenoptera The order Hymenoptera includes wasps, bees, and ants. Wasps, which are found across the United States, live in small colonies and may attack in groups when provoked. Honeybees (*Apis mellifera*) and bumblebees (*Bombus* species), also found across the United States, are generally docile and rarely sting unless provoked. Africanized honeybees (*Apis mellifera scutellata*; also referred to as killer bees) are found primarily in the southwestern states and are far more aggressive than other bees. Fire ants (*Solenopsis invicta* and *Solenopsis richteri*) are wingless, ground-dwelling arthropods that are found in many southern states and attack in an aggressive swarm when provoked.

Although Hymenoptera stingers are small, they can evoke severe local and systemic reactions. The local response to a Hymenoptera sting is a painful, erythematous, and edematous papule that develops within seconds and typically subsides in 4 to 6 hours. Some stingers are barbed and must be removed with a scraping motion, rather than pinching, to prevent the injection of more venom. Systemic reactions occur in about 5% of the population and may lead to anaphylaxis with syncope, bronchospasm, hypotension, and arrhythmias. Wounds and local reactions are treated with ice, elevation, and analgesics. Systemic reactions are treated with subcutaneous epinephrine, diphenhydramine, and supportive airway and blood pressure control.[92] Persons with a history of systemic reactions to insect stings should carry epinephrine kits.

Dressings for Specific Types of Wounds

The functions of a wound dressing include protection, antisepsis, pressure, immobilization, débridement, provision of a physiologic environment, absorption, packing, support, comfort, and aesthetic appearance. More specifically, the functions of a dressing should be tailored to the wound type and the purpose of the dressing must be carefully considered before application. In general, because dry wounds do not epithelialize, a wound with a clean base should be covered with a dressing that retains moisture. If the wound is contaminated or produces a large amount of exudate, an absorptive dressing is needed to remove excess moisture to protect adjacent skin from maceration.

ABRASIONS

Abrasions heal by epithelialization, which is accelerated by the warm, moist environment created by an occlusive dressing.[100,101] Such an environment not only promotes epithelialization but also enhances healing by retaining moisture and a low oxygen tension that promotes the inflammatory phase.[102] A variety of dressings are suitable for treatment of abrasions, including biologic dressings, hydrogels, hydrocolloids, and semipermeable films. These dressings need not be changed as long as they remain adherent. Small, superficial wounds also heal readily when dressed with impregnated gauze dressings (e.g., Xeroform and Scarlet Red, Kendall, Mansfield, MA) that allow exudates to pass through them while maintaining a moist wound bed.[102] These less adherent dressings must be changed more regularly, such as one to two times per day.[103]

Dry dressings (e.g., gauze) should be avoided with abrasions because they facilitate scab formation. Scabs slow epithelialization because advancing cells must enzymatically débride the scab-wound interface to migrate.[104] Wounds covered with a scab also tend to cause more discomfort than wounds covered with occlusive dressings.

LACERATIONS

For sutured wounds, the specific purposes of a dressing are to prevent bacterial contamination, to protect the wound, to manage drainage, and to facilitate epithelialization. Dressings used on such wounds usually consist of three basic layers. The inner (contact) layer is chosen to minimize adherence of the dressing to the wound and to facilitate drainage through itself to the overlying layers. Common choices for this layer include fine-mesh gauze, petrolatum gauze, Xeroform or Xeroflo (Kendall) gauze, and Adaptic (Johnson & Johnson, New Brunswick, NJ). These substances should be applied only as a single layer because when applied in multiple layers, they become occlusive. The middle layer is chosen for absorbency and ability to conform to the shape of the wound. It is usually composed of fluffs, Kerlix (Kendall), or wide-mesh gauze, all of which facilitate capillary action and drainage.[105] Telfa (Kendall) is an example of a simple dressing that combines both a nonadherent layer and an absorbent pad. The middle layer must not become saturated because exudate will collect on the wound surface, causing maceration and possibly bacterial contamination. The outer (binding) layer serves to secure the dressing. Common choices for this layer include Kling (Johnson & Johnson), ACE bandages (BD Medical, Franklin Lakes, NJ), Coban (3M, St. Paul, MN), and Tegaderm (3M).

Dressings are required only until drainage ceases or for 48 hours if draining is minimal. This corresponds with the time that it takes for epithelial cells to seal the superficial layers of the wound. Antibacterial ointments are a viable alternative to dressings in a minimally draining wound [*see* Adjunctive Wound Treatment, Topical Antimicrobials, *above*]. Such ointments are occlusive and maintain a sterile, moist environment for the 48 hours required for epithelialization. In anatomic areas that are difficult to dress (e.g., the scalp), it may be reasonable to forgo a dressing and simply apply ointments or allow a scab to form on the wound surface. Operative wounds are also sometimes covered with an occlusive dressing to optimize epithelialization [*see* Dressings for Specific Types of Wounds, Abrasions, *above*]. Some of these dressings are transparent, allowing observation of the wound. The disadvantage of occlusive dressings is their limited absorptive capacity, which allows drainage from the wound to collect underneath.

COMPLEX WOUNDS

For complex wounds containing necrotic tissue, foreign bodies, or other debris that cannot be removed sharply, wet-to-dry dressings are effective, simple, and inexpensive. A single layer of coarse, wet gauze is applied to a wound, allowed to dry over a period of 6 hours, and removed. Necrotic tissue, granulation tissue, debris, and wound exudate become incorporated within the gauze and are removed with the dressing. The disadvantages of wet-to-dry dressings are pain and possible damage to viable tissue. If the wound bed contains tendons, arteries, nerves, or bone, wet-to-wet dressings should be used to prevent desiccation of these critical structures.

Wet-to-wet dressings, which are not allowed to dry, cause less tissue damage than wet-to-dry dressings. However, they do not produce as much débridement. Most wet-to-wet dressings are kept moist with saline. Wounds with significant bacterial contamination may be treated with dressings that contain antibacterial agents (e.g., Dakin's, mafenide, silver sufadiazine, silver nitrate, or iodine) [*see* Adjunctive Wound Treatment, Topical Antimicrobials, *above*]. Biologic and semipermeable films also maintain a moist wound bed but are difficult to use on deep or irregular wounds and wounds with significant drainage. Enzymatic agents have also been used for wound débridement as an alternative to dressings, but there is a lack of high-quality evidence to guide clinical decisions.[106]

Some wounds are difficult to dress and require special consideration. For wounds with flaps or questionably viable tissue, compression dressings should not be used as they may cause ischemia. Wounds that cross joints are best dressed with plaster splints for temporary immobilization; semipermeable films are flexible and may also be used in this setting. Wounds with high levels of exudates may be dressed with hydrocolloids, hydrogels, or alginates.[102] For large or irregular wounds, NPWT may be beneficial as dressings conform well and remain adherent. Additionally, NPWT uses subatmospheric pressure to remove excess wound fluid, stimulates the formation of granulation tissue, improves peripheral blood flow and tissue oxygenation, reduces the size of the wound, decreases the number of dressing changes, and may even convert a wound not amenable to skin grafting (e.g., exposed bone, tendon, or hardware) to a granulating wound amenable to definitive closure.[37,107,108] Use of NPWT is contraindicated in wounds with exposed blood vessels or bowel due to the risks of vessel desiccation and fistula formation. Although NPWT may be helpful when delayed wound closure is planned,[91] there is no definitive evidence that it leads to better wound healing, and for chronic wounds, there may not be any benefit over simpler dressings.[109]

Postoperative Wound Care

Closed wounds should be kept clean and dry for 24 to 48 hours after repair. Epithelialization begins within hours after wound approximation and forms a barrier to contamination. Tension on the wound should be minimized, and patients should refrain from strenuous activity until the wound has regained sufficient tensile strength. In the first 6 weeks after repair, the wound's tensile strength increases rapidly. After this period, tensile strength increases more slowly, eventually reaching a maximum of 75 to 80% of normal skin strength [*see Figure 2*]. Wounds at risk for infection should be assessed by a medical provider within 48 hours of closure. In addition, the patient should be taught to look for signs of infection (e.g., erythema, edema, pain, purulent drainage, and fever).

The timing of suture or staple removal is determined by balancing the requirements for optimal appearance against the need for wound support. For optimal appearance, sutures should be removed early, before inflammation and epithelialization of suture tracts occur. An epithelialized tract will develop around a suture or staple that remains in the skin for longer than 7 to 10 days. Once the suture or staple is removed, the tract will be replaced by scar.[110] On the other hand, it takes a number of weeks for the wound to gain significant tensile strength, and early removal of wound support can lead to dehiscence of wounds that are under substantial tension. Early suture removal is warranted for some wounds. For example, sutures in aesthetically sensitive areas (e.g., the face) may be removed on day 4 or 5,

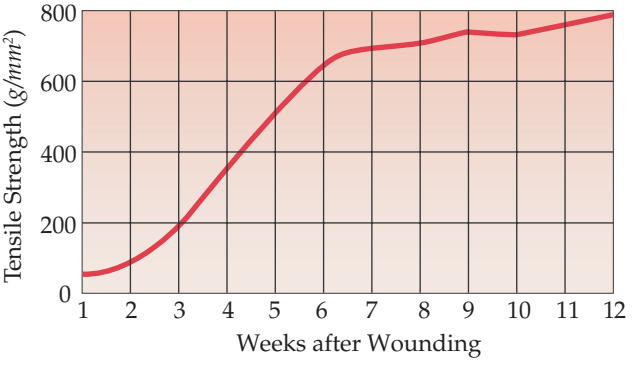

Figure 2 **The tensile strength of skin wounds increases rapidly for approximately 6 weeks after wounding. It then continues to increase slowly for 6 to 12 months, although it never reaches the tensile strength of unwounded tissue. Collagen is remodeled and replaced with highly cross-linked collagen along tissue stress lines. The process of collagen replacement and scar remodeling continues for years.**

and sutures in areas under minimal tension (e.g., in wounds parallel to skin tension lines) may be removed on day 7. Sutures in wounds subject to greater stress (e.g., wounds in the lower extremities or the trunk) should remain in place longer (10 to 14 days), as should sutures in the wounds of patients who have a condition that impairs healing (e.g., malnutrition). In such cases, suture-mark scars are considered acceptable. The appropriate method of removing a suture is first to cut it and then to pull on the knot parallel to or toward the wound. Tapes may then be used to provide further wound support.

After suture removal, numerous methods are available to help minimize scar formation. The cosmetic outcome of a scar is largely determined by the nature and severity of the wound (i.e., degree of dermal and subdermal involvement), which are outside the surgeon's control. The greatest impact a surgeon can have on aesthetic outcome is derived from providing meticulous care when the acute wound is initially encountered. Postoperative wound care therapies to optimize appearance include massage, the use of silicone bandages or pressure garments, and the application of sunscreen or sunblock. These interventions appear to help, but prospective trials are needed to confirm their efficacy and establish treatment guidelines. The healing wound is fragile, and topical application of ointments may have an adverse effect. For example, vitamin E, which is commonly applied to healing wounds, can induce contact dermatitis and cause scars to look worse.[111]

Factors that May Hinder Wound Healing

Despite a surgeon's best efforts, healing does not always occur in an undisturbed fashion. Sometimes, a closed wound dehisces. If the dehiscence is sudden, the wound is clean, and only skin and superficial tissues are involved, then the wound may be reclosed. The cause of the dehiscence should be corrected if possible. If the dehisced wound is contaminated or infected, then the wound should be allowed to heal secondarily, with dressing changes and scar revision to be performed later.

A number of local and systemic factors [*see Table 9*] can interfere with wound healing. Accordingly, it is essential for clinicians to be aware of and knowledgeable about these factors and, whenever possible, to take appropriate measures to improve the chances for optimal healing. The use of nutrients and growth factors to stimulate wound healing may be considered. This measure is currently the subject of extensive research.

LOCAL FACTORS

Tension

Whether from inherent skin tension, poor surgical technique, movement of joints, or inadequate wound support, tension may lead to separation of wound edges. Tension should be minimized by undermining the wound edges during closure. Tissue ellipses from complex wound edges should be kept as narrow as possible and should be created along relaxed skin tension lines. Adequate support of the wound after suture removal is critical. Many surgeons keep tapes (e.g., Steri-Strips) over a wound for 3 weeks until the strength of the wound equals that of the deep sutures and tapes. Wounds over joints should be splinted to reduce tension.

Table 9 Local and Systemic Factors that Impair Wound Healing

Local factors
Tension
Foreign body
Infection
Ischemia
Hematoma and seroma
Trauma
Edema
Irradiation
Systemic factors
Inherited connective tissue disorders
Hypothermia
Oxygen
Tobacco smoking
Malnutrition
Jaundice
Age
Diabetes mellitus
Obesity
Uremia
Steroids
Chemotherapeutic agents
Other drugs

Foreign Body

All foreign bodies should be removed before wound closure. Retained foreign bodies may cause impaired healing, infection, or traumatic tattooing. Iatrogenic foreign bodies may also interfere with wound healing and promote infection. Suture material is a foreign body; thus, the number and size of sutures placed in a wound should be kept to the minimum necessary.

Infection

All traumatic wounds are contaminated and should therefore be irrigated to remove organisms. Infection occurs when bacteria are too numerous ($> 10^5$ organisms/g tissue) or virulent for local tissue defenses to control.[112] As noted [*see* Adjunctive Wound Care, Prophylactic Systemic Antibiotics, *above*], local factors (e.g., impaired circulation and radiation injury) increase the risk of infection, as do various systemic diseases (e.g., diabetes, AIDS, uremia, and cancer). Wound cultures should be obtained, and broad-spectrum antibiotic therapy should be started when infection is diagnosed. The antibiotic regimen is adjusted on the basis of culture results and sensitivities.

Ischemia

Ischemic wound tissue readily becomes infected and therefore must be débrided. Tissue with dermal edges that do not bleed or that show no perfusion on fluorescein testing is ischemic. Questionably viable tissue should be monitored closely and débrided when declared nonviable.

Hematoma and Seroma

Hematomas and seromas increase the risk of infection and the likelihood of wound dehiscence. To prevent their

formation, hemostasis at the time of wound closure must be meticulous, and bleeding diatheses must be corrected. Because the rubbing of wound edges against one another is associated with the formation of hematomas and seromas, wound edge movement should be minimized and immobilization employed as necessary. Wounds at significant risk for hematoma or seroma formation should be closed over a drain.

Large hematomas or seromas that are recognized early (i.e., before infection develops) should be evacuated, and the wound should be reclosed. Small hematomas or seromas can usually be treated conservatively until they are reabsorbed, but close observation is required. If a hematoma or seroma is not recognized until infection has already occurred, the wound should be opened, drained, and allowed to heal secondarily. Scar revision may be carried out at a later point.

Trauma

Tissue injury is obviously associated with external trauma, but it can also be iatrogenic. Rough handling of tissue edges with forceps produces minute crush injuries that may promote wound infection. It is preferable to handle wound edges with hooks using gentle surgical technique.

Edema

Edema results from the accumulation of fluid in the interstitial space. It may occur as an acute process in which tissue injury leads to histamine release, leaky capillaries, and inflammation or as a chronic process in which venous insufficiency, lymphatic insufficiency, and a low plasma oncotic pressure may cause fluid to collect in the interstitium. In both cases, edema raises tissue pressure and inhibits perfusion and healing. The proteinaceous and fibrin-rich fluid also forms clot and fibrous tissue that hinder the supply of oxygen and inflammatory cells.[113] Clearance of wound edema is necessary for healing and may be successfully accomplished by means of compression therapy or NPWT.[107,114]

Irradiation

Radiation damages the skin and can cause wounds to heal slowly. It also induces chronic skin changes, and previously irradiated tissues demonstrate delayed healing.[115] Irradiated tissue is characterized by a thickened and fibrotic dermis, a thin epidermis, pigment changes, telangiectasia, decreased hair, and increased dryness (as a consequence of damage to sebaceous and sweat glands). The microvasculature of the skin is obliterated, leading to tissue ischemia and impaired healing. Keratinocytes, which are necessary for wound epithelialization, exhibit impaired mitotic ability, and slow progressive desquamation (as a consequence of their superficial location and high replication rate) may occur.[113] Collagen bundles become edematous and fibrotic. Fibroblasts, which are necessary for collagen synthesis, also show diminished migration and proliferation.[116]

Because irradiated skin is irreversibly damaged, tissue transfer may be required for repair of wounds in areas subjected to radiation. Vitamin A supplementation can lessen the adverse effects of irradiation on wound healing, and vitamin A may also be helpful in patients on steroids (dose typically 25,000 IU/day).[117]

SYSTEMIC FACTORS

Inherited Connective Tissue Disorders

Several inherited connective tissue disorders interfere with normal wound healing. Ehlers-Danlos syndrome leads to deficient collagen cross-linking that results in lax and fragile skin, lax joints, and impaired wound healing. For example, an Ehlers-Danlos patient who undergoes an elective hernia repair or facelift may have a poor outcome as a consequence of deficient collagen formation and poor wound healing.[118,119] Osteogenesis imperfecta is a procollagen formation disorder that is clinically manifested by brittle bones, increased laxity of ligaments and skin, bone deformities, and impaired wound healing.[120] Marfan syndrome is an autosomal dominant disorder characterized by deficient synthesis of fibrillin, which is a key component in elastin formation. Patients with this syndrome have long extremities and hyperextendable joints. Individuals who are seriously affected have lax ligaments, dissecting aneurysms, dislocated eye lenses, pectus excavatum, and scoliosis. Surgical repair of aneurysms (most commonly aortic) and hernias is usually successful in this population, although healing difficulties may be encountered.[119] Cutis laxa is a disease in which an elastase inhibitor deficiency gives rise to defective elastic tissue. Patients with this disease have thick, coarse, and drooping skin in addition to hernias, aneurysms, heart disease, and emphysema. Unlike patients with the other heritable diseases mentioned, cutis laxa patients often show no impairment of wound healing.[121]

Hypothermia

Hypothermia may develop as a consequence of administration of anesthetic drugs, exposure to cold, or redistribution of body heat. It leads to peripheral vasoconstriction and impaired wound oxygen delivery.[122] Wound tensile strength increases more slowly when healing occurs in a cold environment. Prevention or correction of hypothermia reduces the wound infection rate and increases collagen deposition in patients undergoing abdominal surgery.[123] Preoperative systemic and local warming also reduces the wound infection rate in patients undergoing elective operations.[124] A warm body temperature must be maintained in all wounded patients to reduce subcutaneous vasoconstriction and maximize wound-healing potential.

Oxygen

Tissue oxygenation is necessary for aerobic metabolism, fibroblast proliferation, collagen synthesis and cross-linking, and the antimicrobial oxidative burst of inflammatory cells. Transcutaneous oxygen tension is directly correlated with wound healing.[125] Wound tissue oxygenation is determined by cardiac function, circulating blood volume, arterial inflow, venous drainage, oxygen-carrying capacity of blood (as measured by hemoglobin content), hemoglobin dissociation, and local oxygen consumption.[122,126] Equations describing oxygen delivery are shown below. Each of these variables should be addressed in promoting wound healing.

1. O_2 delivery = CO × Cao_2
2. $Cao_2 = (1.34 \times Hb \times Sao_2) + (0.003 \times Pao_2)$
3. $P_Ao_2 = F_Io_2(P_B - P_{H2o}) - P_Aco_2/R$

where CO = cardiac output, Cao_2 = arterial concentration of oxygen, Hb = hemoglobin, Sao_2 = percent saturation of hemoglobin with O_2, Pao_2 = arterial oxygen tension in mm Hg, P_Ao_2 = alveolar oxygen tension in mm Hg, F_Io_2 = fraction of inspired oxygen, P_B = barometric pressure in mm Hg, P_{H20} = saturated vapor pressure of water, P_Aco_2 = alveolar carbon dioxide tension in mm Hg, R = respiratory quotient.

Supplemental administration of oxygen (inspired or hyperbaric) has been shown to have beneficial effects on wound healing in some studies. The incidence of infection in surgical wounds can be reduced by improving the F_Io_2 with supplemental oxygen.[127] In a study of patients undergoing colon surgery, for example, the wound infection rate was 50% lower when an F_Io_2 of 0.8 was maintained intraoperatively and for 2 hours postoperatively than when an F_Io_2 of 0.3 was maintained.[128] Hyperbaric oxygen therapy (i.e., the delivery of oxygen in an environment of increased ambient pressure) has been used for treatment of many types of wounds in which tissue hypoxia may impair healing.[129] It increases tissue oxygen concentrations 10-fold while also causing vasoconstriction, which results in decreased posttraumatic edema and decreased compartment pressures.[130,131] The elevated pressure and hyperoxia induced by hyperbaric oxygen therapy may promote wound healing. For patients with an acute wound, this modality may be a useful adjunct in treating limb-threatening injury, crush injury, and compartment syndrome.[129]

Circulating volume can be improved by administering crystalloids or blood. However, anemia alone is not associated with impaired wound healing unless it is severe enough to limit circulating blood volume.[132] The vasculature may be compromised either systemically (e.g., by diabetes mellitus or peripheral vascular disease) or locally (e.g., by trauma or scar). Vascular bypass may be necessary to improve tissue oxygenation in patients with poor arterial inflow.[113] Transcutaneous Po_2 monitoring may also help determine care as partial pressure of oxygen in tissue should be maintained above 30 mm Hg to promote proper healing.

Tobacco Smoking

Tobacco smoking reduces tissue oxygen concentrations, impairs wound healing, and contributes to wound infection and dehiscence.[133,134] The effects of smoking are attributable to vasoconstriction (caused by nicotine), displacement of oxygen binding (resulting from the high affinity of carbon monoxide for hemoglobin), increased platelet aggregation,[135] impairment of the inflammatory cell oxidative burst,[136] endothelial damage, and the development of atherosclerosis.[133,134,137] All acutely injured patients should stop smoking, and, ideally, all noninjured patients scheduled to undergo surgery should stop smoking at least 3 weeks before an elective surgical wound is made.[136,138] Like smoked tobacco, transcutaneous nicotine patches alter the inflammatory cell oxidative burst and cause vasoconstriction; accordingly, they, too, should not be used when a wound is present.[136]

Malnutrition

On average, hospitalized patients show a 20% increase in energy expenditure.[113] Good nutritional balance and adequate caloric intake (including sufficient amounts of protein, carbohydrates, fatty acids, vitamins, and other nutrients) are thus necessary for normal wound healing.

All patients who have sustained wounds should undergo nutritional assessment,[139] which typically includes measuring serum levels of albumin, protein, prealbumin, transferrin, and insulinlike growth factor–1 (IGF-1).[113] The serum albumin level is one of the best predictors of operative mortality and morbidity.[140] A value lower than 2.5 g/dL is considered severely depressed, and a value lower than 3.4 g/dL is associated with higher perioperative mortality.[141,142] Protein provides an essential supply of the amino acids used in collagen synthesis, and hypoproteinemia results in impaired healing. Consequently, it is not surprising that protein replacement and supplementation can improve wound healing.[143,144] In particular, supplementation specifically with the amino acids arginine, glutamine, and taurine (which are essential for anabolic processes and collagen synthesis) is thought to enhance wound healing.[145–147] Glutamine is the most abundant free amino acid in the body, and under catabolic conditions, it is released from muscle unless provided as a supplement.

Vitamins C, A, K, and D are essential for normal healing. Vitamin C (ascorbic acid) hydroxylates the amino acids lysine and proline during collagen synthesis and cross-linking. A deficiency of this vitamin causes scurvy, marked by failed healing of new wounds and dehiscence of old wounds. Vitamin C supplementation (100 to 1,000 g/day) can improve wound healing.[113,147] Vitamin A (retinoic acid) is essential for normal epithelialization, proteoglycan synthesis, and normal immune function.[148–150] Retinoids and topical tretinoin may help foster acute wound healing by accelerating epithelialization of full- and partial-thickness wounds, activating fibroblasts, increasing type III collagen synthesis, and decreasing metalloprotease activation.[151,152] Oral retinoid treatment significantly increases the decreased hydroxyproline content, tumor growth factor–β (TGF-β) level, and IGF-1 concentration associated with corticosteroids.[151] In addition, all aspects of corticosteroid-impaired healing—other than wound contraction—can be reversed by providing supplemental oral vitamin A at a recommended dosage of 25,000 IU/day.[153] The retinoic acid derivative isotretinoin (13-*cis*-retinoic acid), however, impairs wound epithelialization and delays wound healing.[154] Vitamin K is a cofactor in the synthesis of coagulation factors II, VII, IX, and X, as well as thrombin. Consequently, vitamin K is necessary for clot formation and hemostasis, the first step in acute wound healing. Vitamin D is required for normal calcium metabolism and therefore plays a necessary role in bone healing.

Dietary minerals (e.g., zinc and iron) are also essential for normal healing. Zinc is a necessary cofactor for DNA and RNA synthesis. A deficiency of this mineral can lead to inhibition of cellular proliferation, deficient granulation tissue formation,[155] and delayed wound healing.[156] Zinc replacement and supplementation can improve wound healing.[147] However, daily intake should not exceed 40 mg

of elemental zinc, because excess zinc can immobilize macrophages, bind copper, and inhibit healing.[157] Iron is also a cofactor for DNA synthesis, as well as for hydroxylation of proline and lysine in collagen synthesis.[113] However, iron deficiency anemia does not appear to affect wound strength.[158]

Jaundice

The effect of jaundice on wound healing is controversial. Jaundiced patients appear to have a higher rate of postoperative wound-healing complications,[159] as well as a lower level of collagen synthesis. However, obstructive jaundice does not affect healing of blister wounds in humans.[160] Jaundiced animals show a significant delay in collagen accumulation within the wound but no significant reduction in the wound's mechanical strength.[161] Biliary drainage may be considered in jaundiced patients with wounds. This measure will improve collagen synthesis, although it may not have any appreciable effect on the healing rate.[160]

Age

Aging has a deleterious effect on the capacity for wound healing.[162] Increasing age is associated with an altered inflammatory response, impaired macrophage phagocytosis, and delayed healing.[163] Nevertheless, even though the wound healing phase begins later and proceeds more slowly compared to younger individuals, elderly patients are still able to heal most wounds.[164]

Diabetes Mellitus

Diabetes mellitus is associated with poor wound healing and an increased risk of infection. Diabetic neuropathy leads to sensory loss (typically in the extremities) and diminished ability to detect or prevent injury and wounding. Once present, wounds in diabetic patients heal slowly. The etiology of this healing impairment is multifactorial. Diabetes is associated with impaired granulocyte function and chemotaxis, depressed phagocytic function, altered humoral and cellular immunity, peripheral neuropathy, peripheral vascular disease, and various immunologic disturbances.[165–168] In addition, it is associated with a microangiopathy that can limit perfusion and delivery of oxygen, nutrients, and inflammatory cells to the healing wound.[169] Diabetes-induced impairment of healing, as well as the attendant morbidity and mortality, may be reduced by tightly controlling blood sugar levels with insulin.[170] Diabetic patients must also closely monitor themselves for wounds and provide meticulous care for any wounds present.

Obesity

Obesity is a growing epidemic in the United States. Not only is obesity often accompanied by diabetes and peripheral vascular disease, the excess weight itself also can lead to shearing forces across the wound and decrease blood flow, which may increase the risk of ischemia, dehiscence, and infection.[24,171]

Uremia

Uremia and chronic renal failure are associated with weakened host defenses, an increased risk of infection, and impaired wound healing.[172] Studies using uremic animal models show delayed healing of intestinal anastomoses and abdominal wounds.[173] Uremic serum also interferes with the proliferation of fibroblasts in culture.[119,173] Treatment of this wound-healing impairment includes dialysis.

Uremic patients with wounds may experience bleeding complications. In this situation, appropriate evaluation includes determining the prothrombin time (PT), the activated partial thromboplastin time (aPTT), the platelet count, and the hematocrit. Treatment includes dialysis without heparin; administration of desmopressin (0.3 μg/kg), cryoprecipitate, conjugated estrogens (0.6 mg/kg/day IV for 5 days),[174] and erythropoietin; and transfusion of red blood cells to raise the hematocrit above 30%.[175,176]

Uremic patients with hyperparathyroidism may also exhibit the uremic gangrene syndrome (calciphylaxis), which involves the spontaneous and progressive development of skin and soft tissue wounds, usually on the lower extremities. Patients with this syndrome typically are dialysis dependent and have secondary or tertiary hyperparathyroidism. Wound biopsies demonstrate fat necrosis, tissue calcification, and microarterial calcification.[177] Treatment includes local wound care, correction of serum phosphate levels with oral phosphate binders,[178] correction of calcium levels with dialysis, and subtotal parathyroidectomy.[177]

Drugs

Steroids Corticosteroids are antiinflammatory agents that inhibit all aspects of healing, including inflammation, macrophage migration, fibroblast proliferation, protein and collagen synthesis, development of breaking strength, wound contraction, and epithelialization.[119,153,179] In the setting of an acute wound that fails to heal, corticosteroid doses may be reduced, vitamin A administered topically or systemically, and anabolic steroids given to restore steroid-retarded inflammation.[119,153]

Unlike corticosteroids, anabolic steroids accelerate normal collagen deposition and wound healing. Oxandrolone is an oral anabolic steroid and testosterone analogue that is employed clinically to treat muscle wasting and foster wound healing and mitigates the catabolism associated with severe burn injury. Supplementation with this agent leads to significant improvements in the wound-healing rate.[180] In burn patients treated with oral oxandrolone, hospital length of stay is significantly reduced and the number of necessary operative procedures is decreased.[181] In ventilator-dependent surgical patients receiving oxandrolone, however, the course of mechanical ventilation is longer than in those not treated with oxandrolone. It has been suggested that the very ability of oxandrolone to enhance wound healing may increase collagen deposition and fibrosis in the later stages of ARDS and thereby prolong recovery.[182] Acute elevation of liver enzyme levels has been seen in some patients treated with oxandrolone; accordingly, hepatic transaminase concentrations should be intermittently monitored in all patients treated with this medication.[181]

Chemotherapeutic agents Both wound healing and tumor growth depend on metabolically active and rapidly dividing cells. Consequently, chemotherapeutic drugs that hinder tumor growth can also impair wound healing. These agents (which include adrenocorticosteroids, alkylating

agents, antiestrogens, antimetabolites, antitumor antibodies, estrogen, progestogens, nitroureas, plant alkaloids, and random synthetics) attenuate the inflammatory phase of wound healing, decrease fibrin deposition, reduce the synthesis of collagen by fibroblasts, and delay wound contraction.[113] Some cytotoxic drugs (e.g., methotrexate and doxorubicin) substantially attenuate the early phases of wound repair and reduce wound strength.[183] The magnitude of these effects is influenced by the timing of the chemotherapeutic agent's delivery in relation to the time when the wound is sustained. Preoperative delivery has a greater adverse effect on healing; for example, doxorubicin impairs wound healing to a greater extent if given before operation than if treatment is delayed until 2 weeks after operation.[184] Chemotherapy also results in myelosuppression and neutropenia that can decrease resistance to infection, allowing small wounds to progress to myonecrosis and necrotizing soft tissue infections.[185] In all acutely wounded patients who have recently been treated with, are currently taking, or will soon begin to take chemotherapeutic agents, the wounds must be closely observed for poor healing and complications.

Other drugs Many other commonly used drugs affect wound healing and thus should be avoided in the setting of an acute wound. Nicotine, cocaine, ergotamine, and epinephrine all cause vasocontriction and tissue hypoxia. Nonsteroidal antiinflammatory drugs (e.g., ibuprofen and ketorolac) inhibit cyclooxygenase production and reduce wound tensile strength. Colchicine decreases fibroblast proliferation and degrades newly formed extracellular matrix. Antiplatelet agents (e.g., aspirin) inhibit platelet aggregation and arachidonic acid–mediated inflammation. Heparin and warfarin impair hemostasis by virtue of their effects on fibrin formation.[108,186,187] As noted [*see* Factors that May Hinder Wound Healing, Systemic Factors, Malnutrition, *above*], isotretinoin inhibits wound epithelialization and delays wound healing.[154] Vitamin E (α-tocopherol) impairs collagen formation, inflammation, and wound healing,[188] and topical application of this agent can cause contact dermatitis and worsen the cosmetic appearance of scars.[111]

Discussion

PHYSIOLOGY OF WOUND HEALING

Wound healing is not a single event but a continuum of processes that begin at the moment of injury and continue for months. These processes take place in the same way throughout the body and for the purposes of description may be broadly divided into three phases: (1) inflammation, (2) migration and proliferation, and (3) remodeling [*see Figure 3*]. Humans, unlike salamanders, for instance, lack the ability to regenerate specialized structures; instead, they heal by forming a scar that lacks the complex and important skin structures seen in unwounded skin [*see Figure 4*].

Inflammatory Phase

The inflammatory phase of wound healing begins with hemostasis followed by the arrival of neutrophils and then macrophages [*see Figure 5*]. This response is most prominent during the first 24 hours. Signs of inflammation are erythema, edema, heat, and pain. These are generated primarily by changes in the venules on the distal side of the capillary bed. In clean wounds, signs of inflammation dissipate relatively quickly, and few, if any, inflammatory cells are seen after 5 to 7 days. In contaminated wounds, inflammation may persist for a prolonged period.

Because wounds bleed when blood vessels are injured, hemostasis is essential. In the first 5 to 10 minutes after wounding, platelets aggregate and release dense and alpha granules. Dense granules contain vasoactive substances that induce vasoconstriction, contributing to hemostasis, and the skin blanches as a result. Vasoconstriction is mediated by catecholamines (e.g., epinephrine and norepinephrine) and prostaglandins (e.g., prostaglandin $F_{2\alpha}$ [$PGF_{2\alpha}$] and thromboxane A_2 [TXA_2]). As vessels contract, platelets continue to aggregate and adhere to the blood vessel collagen exposed by the injury. Aggregating platelets release alpha-granule proteins that result in further platelet aggregation and trigger further cytokine release. The growth factors and cytokines involved in cutaneous wound healing include epidermal growth factors, fibroblast growth factors, transforming growth factor–β (recruits neutrophils and T cells and stimulates collagen production by fibroblasts), platelet-derived growth factor (exerts chemotactic, activating, and mitogenic effects on neutrophils, fibroblasts, smooth muscle cells, and macrophages), vascular endothelial growth factor (VEGF), tumor necrosis factor–α (TNF-α), interleukin-1 (IL-1), IGF-1, granulocyte colony-stimulating factor, and granulocyte-macrophage colony-stimulating factor.[189] Some of these cytokines have direct effects early in the healing process; others are bound locally and play critical roles in later healing phases. The use of specific cytokines to reverse healing deficits or promote wound healing appears to be a promising clinical tool and is currently the subject of ongoing basic scientific and clinical research.[190] Currently, platelet-derived growth factor is the only topical growth factor approved by the Food and Drug Administration that is used in the treatment of chronic wounds. Cellular therapy research with mesenchymal stromal cells and endothelial progenitor cells is another example of active research.

The coagulation cascade also contributes to hemostasis. The extrinsic pathway is essential to hemostasis and is stimulated by the release of tissue factor from injured tissue. The intrinsic cascade is not essential and is triggered by exposure to factor XII. Both coagulation pathways lead to the generation of fibrin, which interacts with platelets to form a clot in the injured area. Fibrin both contributes to hemostasis and is the primary component of the provisional matrix [*see* Physiology of Wound Healing, Migratory and Proliferative Phase, Provisional Matrix Formation, *below*].

Vasoconstriction and hemostasis are followed by vasodilatation, which is associated with the characteristic signs of inflammation. Vasodilatation is mediated by prostaglandins (e.g., PGE_2 and PGI_2 [prostacyclin]), histamine, serotonin, and kinins.[191–193] As the blood vessels dilate, the endothelial cells separate from one another, thereby increasing vascular permeability. Inflammatory cells initially roll along the endothelial cell lining, subsequently undergo integrin-mediated adhesion, and finally transmigrate into the extravascular space.[192]

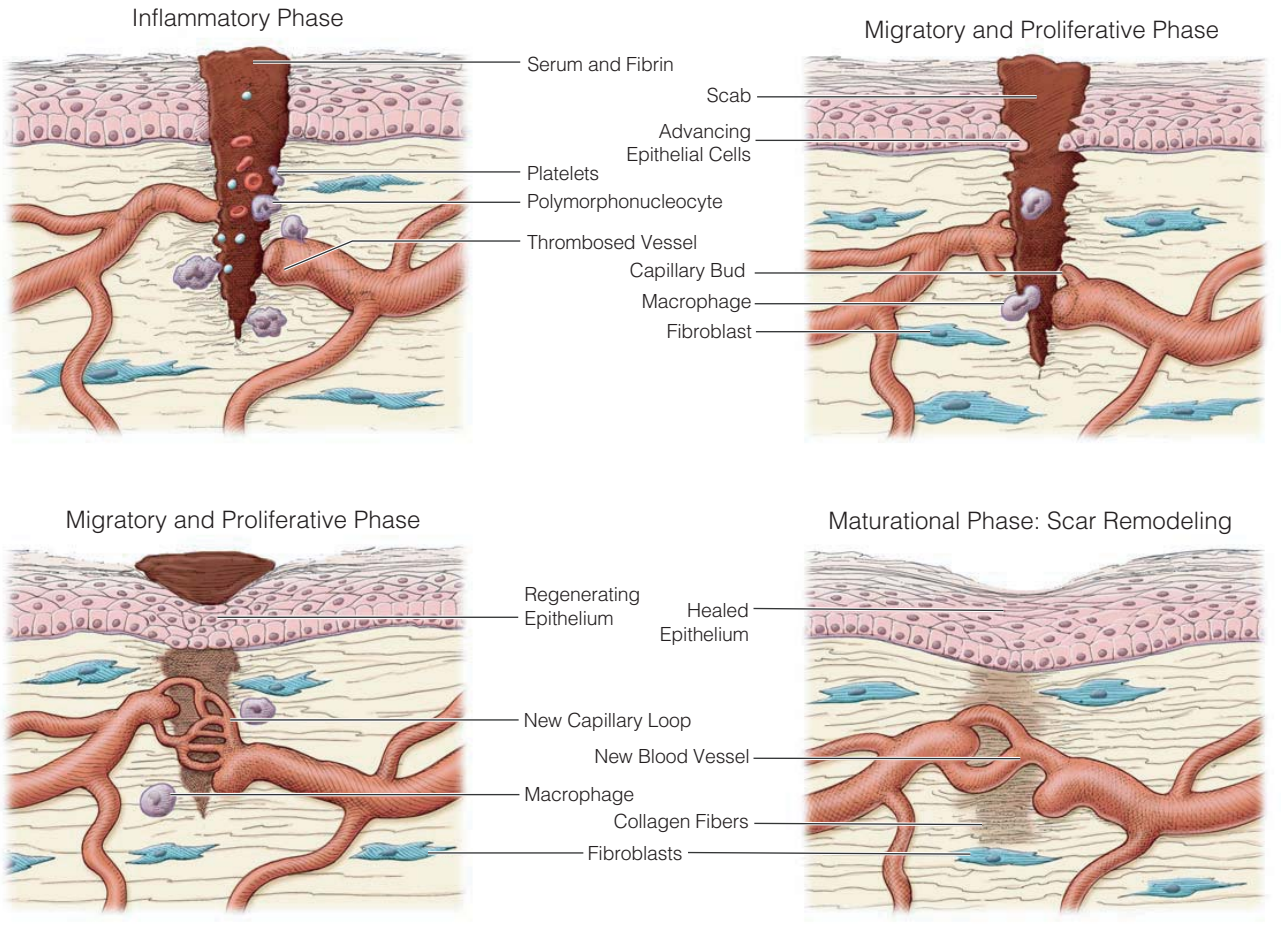

Figure 3 **The phases of wound healing. In the inflammatory phase (*top*, *left*), platelets adhere to collagen exposed by damage to blood vessels to form a plug. The intrinsic and extrinsic pathways of the coagulation cascade generate fibrin, which combines with platelets to form a clot in the injured area. Initial local vasoconstriction is followed by vasodilatation mediated by histamine, prostaglandins, serotonin, and kinins. Neutrophils are the predominant inflammatory cells (a polymorphonucleocyte is shown here). In the migratory and proliferative phase (*top*, *right*; *bottom*, *left*), fibrin and fibronectin are the primary components of the provisional extracellular matrix. Macrophages, fibroblasts, and other mesenchymal cells migrate into the wound area. Gradually, macrophages replace neutrophils as the predominant inflammatory cells. Angiogenic factors induce the development of new blood vessels as capillaries. Epithelial cells advance across the wound bed. Wound tensile strength increases as collagen produced by fibroblasts replaces fibrin. Myofibroblasts induce wound contraction. In the maturational phase (*bottom*, *right*), scar remodeling occurs. The overall level of collagen in the wound plateaus; old collagen is broken down as new collagen is produced. The number of cross-links between collagen molecules increases, and the new collagen fibers are aligned so as to yield an increase in wound tensile strength.**

For the first 48 to 72 hours after wounding, neutrophils are the predominant inflammatory cells in the wound. About 48 to 96 hours after wounding, monocytes migrate from nearby tissue and blood and transform into macrophages, eventually becoming the predominant inflammatory cells in the wound, typically by 72 hours. Both neutrophils and macrophages engulf damaged tissue and bacteria and digest them. After neutrophils phagocytose damaged material, they cease to function and often release lysosomal contents, which can contribute to tissue damage and a prolonged inflammatory response. Macrophages are essential to wound healing and unlike neutrophils do not cease to function after phagocytosing bacteria or damaged material.[194] In the wound environment, macrophages also secrete collagenase, elastase, and matrix metalloproteinases (MMPs) that break down damaged tissue. Macrophages also produce cytokines that mediate wound-healing processes, as well as IL-1 (which can lead to a systemic response, including fever) and TNF-α.[189]

Migratory and Proliferative Phase

The migratory and proliferative phase is marked by the attraction of epidermal cells, fibroblasts, and endothelial cells to the wound. Cells migrate along the scaffolding of fibrin and fibronectin. This process involves the upregulation of integrin receptor sites on the cell membranes, which allows the cells to bind at different sites in the matrix and pull themselves through the scaffolding. Migration through the provisional matrix is facilitated by proteolytic enzymes. Cytokines and growth factors then stimulate the proliferation of these cells.[189,194]

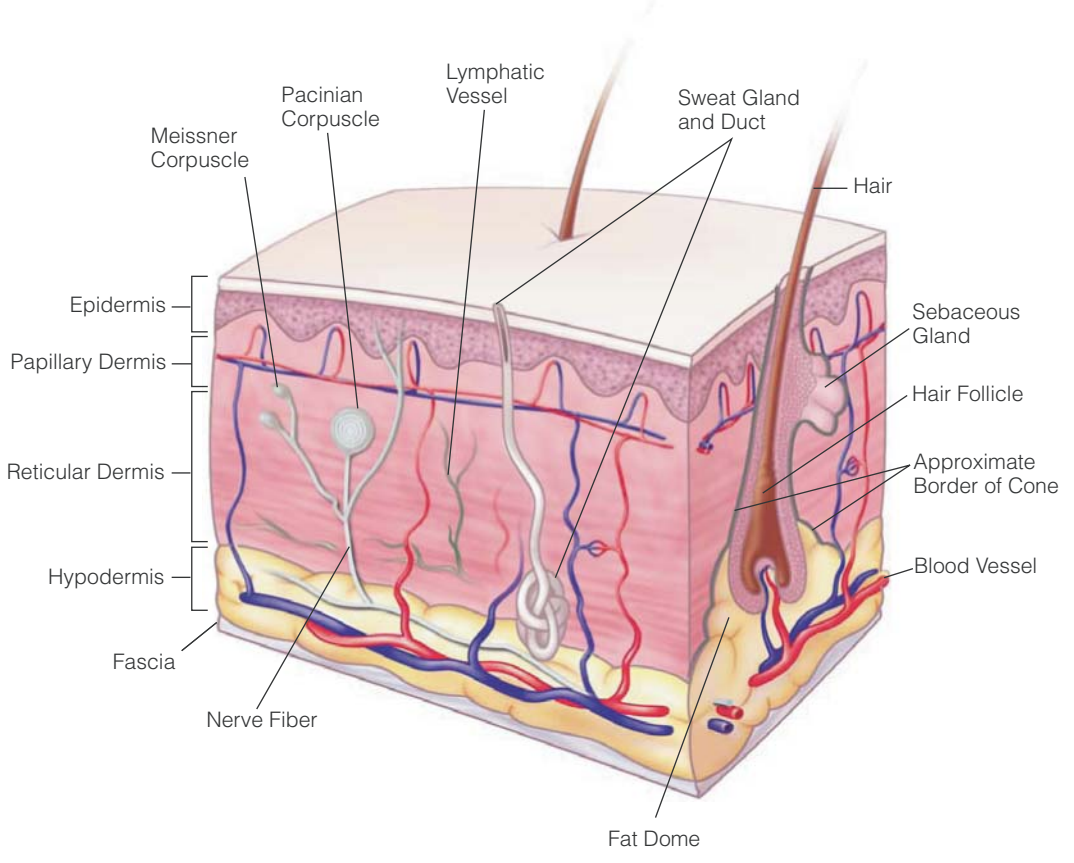

Figure 4 **Key anatomic components of the skin.**

Epithelialization Within approximately 24 hours of injury, epidermal cells from the wound margin and skin appendages begin to migrate into the wound bed. These migrating epidermal cells dissect the wound, separating desiccated eschar from viable tissue.[104] At 24 to 48 hours after wounding, epidermal cells at the wound margin begin to proliferate, producing more migrating cells.[189] As epidermal migration is initiated, the desmosomes that link epidermal cells together and the hemidesmosomes that link the epidermal cells to the basement membrane disappear.[195] Migrating epidermal cells express integrin receptors that allow interaction with extracellular matrix proteins, laminin, collagen, and fibrin clot.[196] When epidermal cells migrating from two areas meet, contact inhibition prevents further migration. The cells making up the epidermal monolayer then differentiate, divide, and form a multilayer epidermis. For incisional wounds closed primarily, reepithelialization is typically complete within 24 to 48 hours.

Angiogenesis and vasculogenesis The growth of new blood vessels begins 2 to 3 days after wounding to support the healing tissue. Angiogenesis is the growth of new blood vessels from existing vessels, whereas vasculogenesis is the de novo formation of blood vessels from endothelial progenitor cells. This process of neovascularization may be stimulated by the hypoxic and acidic wound microenvironment as well as by cytokines (e.g., VEGF) released from epidermal cells and macrophages.[189,197] Endothelial cells from surrounding vessels express fibronectin receptors and grow into the provisional matrix. These migrating endothelial cells create paths in the matrix for developing capillaries by releasing plasminogen activator, procollagenase, heparanase, and MMPs that break down fibrin and basement membranes.[189,198] The budding capillaries join and initiate blood flow. As the wounded area becomes better vascularized, the capillaries consolidate to form larger blood vessels or undergo apoptosis.[199] It is during this phase that the granulation tissue begins to develop, classically described as beefy red tissue. This serves as a sign that the proliferative phase is beginning to predominate.

Provisional matrix formation Formation of the provisional matrix and granulation tissue begins approximately 3 to 4 days after wounding. Lymphocytes begin to predominate around days 4 to 7 and release cytokines, mediating the inflammatory response. T cells are critical to normal wound healing, as demonstrated by the fact that immunosuppressive regimens targeting T cells have detrimental effects on the healing process. Fibroblasts synthesize an extracellular matrix of fibrin, fibronectin, and proteoglycans that supports epidermal and endothelial cell migration and proliferation.[196,200] Proteoglycans (e.g., dermatan sulfate, heparin, heparan sulfate, keratan sulfate, and hyaluronic acid) consist of a protein core that is linked to one or more glycosaminoglycans that anchor proteins and facilitate the alignment of collagen into fibrils.

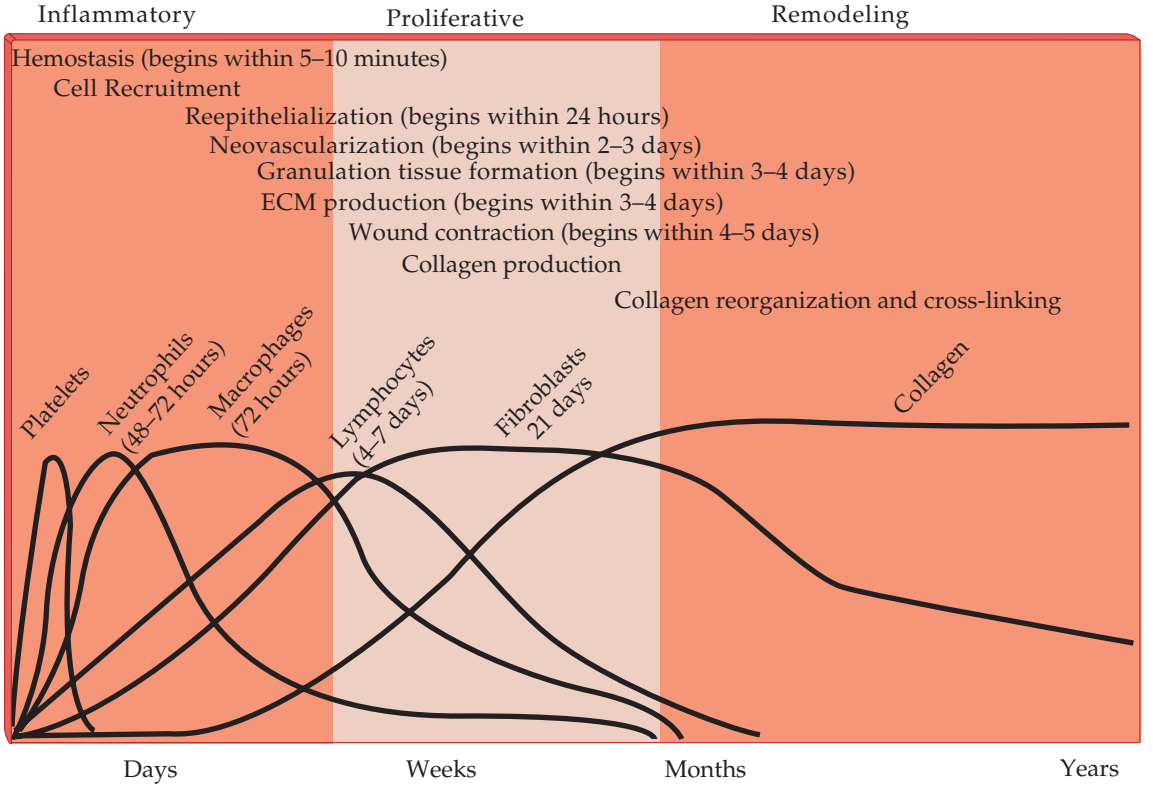

Figure 5 **The phases of wound healing. The inflammatory phase begins within 5 to 10 minutes after wounding with the arrival of platelets. The release of cytokines and chemokines signals other cells to migrate to the injured area. Neutrophils arrive next to engulf damaged material and are soon followed by the arrival of macrophages. Damaged tissue is broken down, and soon epidermal cells, fibroblasts, and endothelial cells migrate to the wound, signaling the beginning of the proliferative phase. Fibroblasts then begin replacing the provisional extracellular matrix (ECM) with a collagen matrix, and the wound gains strength. The rate of collagen synthesis continues at an increased rate for 21 days before gradually declining, marking the beginning of the remodeling phase. Adapted from Figure 1.2 in Herdrich B. Liechty K. Wound healing. In: Porrett P, Frederick J, Roses R, Kaiser L, editors. The surgical review. An integrated basic and clinical science study guide. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2010. p. 4.**

Fibrin becomes coated with vitronectin and fibronectin, which are glycoproteins that facilitate the adhesion of migrating fibroblasts and other cells to the provisional extracellular matrix.[201] By influencing cellular attachment, fibronectin helps modulate cell migration into the wound.[202] In addition, the fibrin-fibronectin lattice binds various cytokines that are released at the time of injury and serves as a reservoir for these factors in the later stages of healing.[203]

Fibroblasts then replace the provisional extracellular matrix with a collagen matrix, and the wound gains strength. The rate of collagen synthesis increases greatly after the initial 3 to 5 days and continues at an increased rate for 21 days before gradually declining.[204] Of the many types of collagen, the ones that are of primary importance in the skin are types I and III. Approximately 80 to 90% of the collagen in the skin is type I collagen; the remaining 10 to 20% is type III. The percentage of type III collagen is higher in embryonic skin and in skin that is in the early stages of wound healing. During remodeling, the type III collagen is replaced by type I collagen.

Collagen molecules are synthesized by fibroblasts. Lysine and proline residues within the collagen molecule become hydroxylated after being incorporated into polypeptide chains. This process requires specific enzymes as well as various cofactors (i.e., oxygen, vitamin C, α-ketoglutarate, and ferrous iron). The result is procollagen, which is released into the extracellular space. Individual collagen molecules then align and associate with one another to form fibrils. Covalent cross-links form between various combinations of the hydroxylated residues (lysine and hydroxylysine) in aligned collagen fibrils, with the strongest links occurring between hydroxylysine and hydroxylysine residues. These cross-links are essential to the tensile strength of the wound. Cofactor deficiencies (e.g., vitamin C deficiency in scurvy) and the use of corticosteroids can lead to the synthesis of weak, underhydroxylated collagen that is incapable of generating strong cross-links.

Wound contraction Myofibroblasts are specialized fibroblasts containing alpha–smooth muscle actin microfilaments that contribute to wound contraction.[205,206] The wound edges are pulled together by the contractile forces supplied by the myofibroblast. Wound contraction generally begins in the 4- to 5-day period after wounding and continues for 12 to 15 days or until the wound edges meet. The rate at which contraction occurs varies with the laxity of the tissue

and is highest at anatomic sites with redundant tissue. Excessive contraction can lead to contracture, a pathologic scarring that impairs the function and appearance of the scar.

Remodeling Phase

Collagen remodeling begins approximately 3 weeks after wounding. Collagen synthesis is downregulated, and the rates at which collagen is synthesized and broken down reach equilibrium. The wound becomes less cellular as apoptosis occurs. During this process, the extracellular matrix, including collagen, is continually remodeled and synthesized in a more organized fashion along stress lines.[204] Collagen breakdown is mediated by MMPs, and the number of cross-links between collagen fibers increases.[198,207] The realigned and highly cross-linked collagen is much stronger than the collagen produced during the earlier phases of healing. The tensile strength of the wound increases rapidly for 6 weeks after injury, and during this period, heavy lifting and any other activity that applies stress across the wound should be avoided. After the initial 6 weeks, tensile strength increases more slowly for a further 6 to 12 months, although it never reaches the tensile strength of unwounded tissue [*see Figure 2*]. TGF-β's effects on increasing collagen and decreasing extracellular matrix degradation result in increased collagen formation; thus, TGF-β has been linked to the development of pathologic fibrosis and hypertrophic scarring.

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Acknowledgments

Figures 1 and 4 Thom Graves
Figure 2 Janet Betries
Figure 3 Carol Donner