Chapter 10

MEDICAL ISSUES IN THE CARE OF THE COMBAT AMPUTEE

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ISSUES IN INFECTIOUS DISEASES

Management of Infectious Issues in the Combat Amputee/Extremity Trauma Patient

Prophylactic Antibiotics for the Combat Amputee/ Extremity Trauma Patient

Throughout the history of warfare, open extremity fractures have been associated with significant morbidity and mortality. Field surgeons used therapeutic amputations as a last line of defense against sepsis and exsanguination with poor results. During the Franco–Prussian War, management of these injuries accounted for 13,173 amputations with 10,006 reported deaths.[1] During the American Civil War, the mortality rate for lower extremity fractures ranged from 14% to 32%, despite approximately 29,980 amputations reported. Early in World War I an open femoral fracture carried a mortality risk of 80%; however, mortality was reduced to 16% with the advent of the Thomas traction splint.[2] Further advancement in fracture reduction, splinting, surgical debridement, and subsequent healing by secondary intention contributed to even better outcomes. The importance of debridement in decreasing septic mortality from wounds was demonstrated in both the Spanish Civil War and World War I. [2] The often-cited surgeon's creed "cut to cure" should not be dismissed or maligned because this philosophy led to markedly improved survival rates during the preantibiotic era and continues to play a significant part of battlefield injury management in the modern age of broad-spectrum antibiotics and multidrug-resistant organisms (MDROs).

With the discovery of penicillin and subsequently streptomycin and the sulfonamides, physicians anticipated that patient outcomes would improve. Yet, it became evident that even with antibiotics, closure of an infected wound was still prone to failure. Delayed primary closure of an infected wound has evolved into common practice of battlefield medicine. Although it is universally accepted to use antibiotics to treat an infected wound, its use to prevent wound infection is not as clearly defined and may contribute to antibiotic-resistant bacteria.

For 50 years, various prophylactic regimens have been used with varied success. A majority of the data comes from civilian literature and may not always apply to the combat injured. In 1974 Patzakis et al reported the first prospective randomized data demonstrating the effectiveness of prophylaxis in wound infections.[3] Since this report several studies and guidelines have addressed it. In this chapter these data will be reviewed and a framework for the prevention of wound sepsis will be presented.

Initially, the wound should be grossly decontaminated without compromising hemostasis. The wound is then protected with a sterile or clean dressing and orthosis depending on the wound location (ie, wrist hand orthosis on an open distal ulnar fracture). The patient is triaged and transitions through higher levels of care with further wound management to include incision and drainage/debridement and definitive surgical treatment. Tetanus prophylaxis should be provided and documented if not up-to-date or unknown. Although it is mandatory for US service members to have up-to-date tetanus immunization before deployment, this may not be the case for allied soldiers or injured noncombatants.

Characteristics of a fracture determine the risk of infection. The commonly used Gustilo classification scheme for open fractures provides a useful tool for standardizing care, predicting potential complications, and comparing similar injuries in published reports.[4]

There is little value to culturing wounds early in the clinical course. In a series of 1,104 open fractures that were swabbed for aerobic/anaerobic culture before administration of antibiotics, 7% of the positive surveillance wound cultures developed infection with the same bacterium.[5] Another series of 89 consecutive open fractures demonstrated 83% initial surveillance culture growth, but after debridement, 60% of repeat cultures were negative or grew nonpathogenic bacteria.[6] Most wounds at presentation (before debridement/therapeutic irrigation) are colonized or contaminated, but rarely develop true infection. The authors recommend only obtaining wound cultures and initiating antibiotic treatment when clinical symptoms/findings indicate a true infection, such as fever, elevated white blood cell count, change in vital signs, purulent discharge, etc.

Pre- and perioperative antibiotic prophylaxis has repeatedly demonstrated reduced postoperative infectious complications.[7] Significant variation persists in antibiotic selection, timing, and duration of administration. The Surgical Infection Prevention Project guidelines address this topic[8]:

1. *Timing of the first dose of antimicrobial therapy*. The first dose should begin within 60 minutes of the incision. If a fluoroquinolone or vancomycin is used, infusion should begin within 120 minutes of incision to reduce antibiotic-associated reactions. If a proximal tourniquet is used, administering the full antibiotic dose before tourniquet application is desirable.

2. *Duration of antimicrobial prophylaxis*. No compelling evidence indicates that the use of antibiotics until all catheters and drains are removed will lower infection. Prophylactic antimicrobials should be discontinued within 24 hours postoperatively.

Orthopaedic surgical prophylaxis regimens typically involve first or second generation cephalosporins (excellent coverage for anticipated community-based skin flora). Suggested regimens for total joint (hip and knee) arthroplasty are cefazolin 1 to 2 grams intravenous (IV) or cefuroxime 1.5 gram IV. These also would be appropriate for amputation prophylaxis. Vancomycin 1 gram IV may be used if a beta-lactam allergy/intolerance exists. These recommendations should be considered with each hospital's antibiogram (local sensitivities and resistance patterns) because the presence of MDROs may influence the appropriate choice. Consultation with departments of infectious disease, infection control, and surgical services is recommended.

Management of Infectious Issues in Combat Amputee/Extremity Trauma Patients at a Military Tertiary Care Center

War Wound Infections and Appropriate Antibiotic Therapy

The bacteriology of war wounds has changed significantly over the past 100 years. During World War I, *Streptococcus spp* and *Clostridium spp* predominated. Wound infections in World War II showed anaerobic organisms and skin flora such as *Streptococcus spp* and *Staphylococcus aureus*. With the advent of antibiotics and improved wound debridement techniques, there has gradually been a shift to gram-negative wound infections during the Vietnam and Korean wars. Organisms such as *Enterobacter spp*, *Escherichia spp*, *Klebsiella spp*, *Pseudomonas spp*, and present-day *Acinetobacter baumannii-calcoaceticus* complex (ABC) have begun to emerge as predominant pathogens of battle wounds.[9,10]

More than 18,000 service members were injured from 2001 to 2006 while serving in Afghanistan and Iraq. The prevalence of extremity wounds with concomitant infection has been high.[9,10] Murray et al examined wound culture isolates from soldiers admitted to a combat support hospital in Baghdad, Iraq, at the time of initial injury.[11] Of 61 soldiers, 30 (49%) had positive wound cultures, predominantly composed of less pathogenic gram-positive skin commensals (2 cases of which were methicillin-resistant *Staphylococcus aureus* [MRSA]). Of the three gram-negative organisms isolated, all were drug sensitive. The lack of drug resistance and decreased pathogenicity supported the curtailment of the use of broad-spectrum prophylactic antibiotics in theater.[11]

In contrast to Murray's findings within the theater, wound and blood cultures taken at tertiary care facilities showed increasing gram-negative bacteria, particularly MDROs.[9,10] A report to the Centers for Disease Control and Prevention (CDC) in 2004 demonstrated increasing rates of drug-resistant ABC as a cause of bloodstream infections in 102 soldiers injured in Iraq, Kuwait, and Afghanistan that were treated at military medical tertiary care facilities.[12] Petersen et al identified major pathogens isolated from war trauma-associated infections in 56 soldiers on the USS Comfort from March through May 2003.[10] Of wound cultures obtained, 47% were polymicrobial with ABC the predominant organism (33%), followed by *Escherichia coli* (18%), and *Pseudomonas spp* (17%). Overall, 81% of organisms in wound cultures were gram-negative bacteria, whereas 19% were gram-positive bacteria. Aronson et al reported similar data from Walter Reed Army Medical Center (WRAMC) with ABC, *Pseudomonas aeruginosa, E coli,* and *Klebsiella spp* accounting for a majority of war wound infections.[9] Recent evidence suggests that the outbreak of multidrug-resistant ABC infection in the US military healthcare system likely results from environmental contamination of field hospitals coupled with broad-spectrum antibiotic use and transmission within healthcare facilities.[13]

According to the CDC/Healthcare Infection Control Practices Advisory Committee 2006 guidelines, MDROs are defined as resistant to one or more classes of antibiotics.[14] MDROs such as MRSA, ABC, and extended-spectrum beta-lactamase (ESBL) producing organisms are being isolated from wound infections and other sterile body sites and fluids in soldiers.[9,10,12] The incidence of multidrug-resistant ABC in all culture sites at WRAMC increased from 0.087 cases per 1,000 admissions in 2002 to 0.3 cases per 1,000 admissions in 2005.

Treatment of war wound infections primarily involves surgical debridement of devitalized tissue with adjunctive antibiotics. Antibiotic susceptibility testing must guide treatment for MDROs. Currently, ABC susceptibility testing has increased utilization of polymyxins, carbapenems, and aminoglycosides for treatment.[9,10,12] Severely ill or immunocompromised patients with multidrug-resistant ABC infection have been treated with combination therapy based on in-vitro and some in-vivo reports of synergy with combinations of polymyxins with rifampin and/or

carbapenems; however, the clinical relevance of these data remains uncertain.[15,16] A carbapenem is typically the preferred drug for treating ESBL organisms.[17,18] Multiple drugs are available to treat MRSA infections such as vancomycin, linezolid, and trimethoprim-sulfamethoxazole.

The decision to treat war wound cultures and the duration of treatment are challenging. These decisions are dependent on the clinical suspicion for infection and type of infection present (ie, superficial vs deep infection). When MDROs are isolated from sterile sites, an infectious disease specialist should be consulted for further treatment recommendations.

Management and Follow-Up of Surgical Infections for Combat Amputee/Extremity Trauma Patients

Colonization

In postsurgical patients, differentiating between colonization and true infection is critical. Colonization is defined as the isolation of microorganisms in culture without accompanying clinical signs and symptoms of infection. The presence of the organism is not pathogenic and treatment is usually not required because of the lack of active infection, although antimicrobial measures are sometimes undertaken to decolonize a patient for infection control purposes (discussed below). To avoid unnecessary antibiotic use, the authors recommend against culturing wounds and surgical sites without clinical signs or symptoms of infection.

Surgical Site Infections. Surgical site infections (SSIs) are the most common complication of hospitalized surgical patients.[19] Risk for the development of SSIs is related to both patient and operation characteristics. Contaminated and high-risk surgeries are associated with higher frequency of SSI development, with amputations among the highest risk procedures.[20] Organisms commonly causing orthopaedic procedure-associated SSIs include *S aureus*, coagulase-negative staphylococcal species, and gram-negative bacilli. Surveillance data demonstrate that the epidemiology of SSIs in critically ill patients has been changing: the percentage of SSIs associated with gram-negative bacilli decreased from 56.5% in 1986 to 33.8% in 2003. The distribution of gram-negative pathogens also has changed, with decreasing numbers of *E coli* and *Enterobacter* isolates and an increase in the frequency of *Acinetobacter*-associated SSIs.[21] *Acinetobacter spp* and ESBL-producing organisms have presented a particularly difficult clinical challenge to US military hospitals because of high levels of antimicrobial resistance among those pathogens.

SSIs are categorized as follows:

- superficial incisional SSI,
- deep incisional SSI, and
- organ/space SSI.[22]

As defined for surveillance purposes, superficial incisional SSIs occur within 30 days of the operation, involve only the skin or subcutaneous tissue of the incision, and feature at least one of the following: (1) purulent drainage; (2) organisms isolated from culture of fluid or tissue from the incision; (3) local signs or symptoms to include pain or tenderness, swelling, erythema, and warmth; and (4) diagnosis by the surgeon or attending physician.

Deep incisional SSIs occur within 30 days of the operation (within 1 year if an implant is in place); involve the deep soft tissues (muscle and fascial layers) of the incision; feature at least one of the four characteristics listed in the previous paragraph; and involve the patient with a fever greater than 38° Celsius or evidence of abscess or other infection on examination, histopathology, or radiologic examination.

Organ/space SSIs occur within 30 days after the operation if no implant is in place or within 1 year if an implant is in place and involve part of the anatomy that was opened or manipulated. In patients undergoing amputations, the organ/space SSI includes joint or bursa infections and osteomyelitis. Organ/space SSIs are usually treated as infections related to the relevant organ and space, whereas the superficial and deep incisional SSIs are treated as skin and soft tissue infections.

The diagnosis of an SSI is made with emphasis on examination of the incision. Signs of infection include tenderness, swelling, erythema, and purulent drainage. Clinical manifestations of SSIs typically occur 5 days postoperatively. Fever within the first 48 hours postoperatively is only rarely attributable to SSI.[23] Exceptions include SSIs resulting from streptococci and clostridial organisms, which can be diagnosed by the Gram stain of incisional drainage, and staphylococcal toxic shock syndrome, which is accompanied by the early findings of fever, hypotension, elevated liver-associated enzymes, and diarrhea.[24] In the presence of early postoperative fever, the incision should be examined thoroughly and any drainage should be sampled, and a thorough evaluation of all potential causes of common nosocomial infections should be conducted.

The Infectious Diseases Society of America has published guidelines for SSI treatment.[25] The most important aspect of treating SSIs is to open the wound, remove infected material, and perform dressing changes

until the wound heals by secondary intention. Following drainage of the wound, antibiotic administration is not recommended without evidence of invasive infection or systemic illness. However, in patients with fever ($>38.5^{o}$ Celsius) or tachycardia, a short course of antibiotics may be indicated (24–48 hours). The choice of therapy is often empiric, but should be guided by Gram stain or culture results when available. *S aureus* and streptococcal species are the most common infecting pathogens in SSIs following clean procedures (those procedures not entering the gastrointestinal or genital tracts). Consequently, agents with gram-positive coverage such as cefazolin, oxacillin, and clindamycin are recommended. Surgical procedures involving the gastrointestinal and genitourinary tracts as well as incisions involving the axilla or perineum have a higher incidence of gram-negative organisms and anaerobic pathogen infections. In these circumstances, effective choices include cefotetan, ampicillin/sulbactam, or a fluoroquinolone plus clindamycin. In all cases in which the rate of MRSA infection is high, vancomycin or linezolid should be considered while awaiting results of culture and susceptibility testing. In the authors' experience with patients returning from Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF), limited-spectra antibiotics have been less useful because of the prevalence of MDROs. Antimicrobials with broader spectra have been required for these wound infections and should be considered as empiric therapy in clinically severe infections.[26]

Implant Infections. SSIs may affect surgical implants. Implant-associated infections occur perioperatively by bacterial contamination during surgery, by hematogenous spread of pathogens through blood from a distant infectious focus, or contiguously from an adjacent infectious focus.[27] Definitive diagnosis of implant-associated infection involves the presence of clinical manifestations, intraoperative signs of infection adjacent to the implant, and the growth of pathogens in cultures of surgical specimens.[28] A full discussion of device-related infections is beyond the scope of this chapter but an overview is provided below.

For infections related to an implanted orthopaedic device, the surgical treatment has traditionally involved resection arthroplasty or removal of the fixation device. The surgical management of infected joint prostheses varies from debridement with prosthesis retention to two-stage replacement, which involves hardware removal, followed by the placement of an antimicrobial-containing spacer. The patient undergoes a prolonged course of systemic antibiotics—typically 6 weeks—and subsequent implantation of a new prosthesis. The two-stage replacement approach is preferred over the one-stage approach because of improved cure rates and superior functional outcomes.[29]

Infections of fracture-fixation devices that involve bone, including pin-site infections, are treated as osteomyelitis with a 6-week course of systemic antibiotics. Superficial infections of these devices can be adequately treated with 10 to 14 days of antibiotic therapy once the possibility of deeper infection has been excluded. Surgical intervention depends on the type of device, the presence of bone union, and the clinical stability of the patient. Infection of intramedullary nails usually requires removal of the infected nail, use of external-fixation pins, and potentially subsequent insertion of a replacement nail. Surgical intervention of infected external-fixation pins[28] involves removing infected pins and, if bone union has not occurred, inserting new pins at a distant site or fusion of the bones.

In the authors' experience, a large number of patients with orthopaedic implant infections have not been able to undergo immediate device removal because of the extent of their injuries. In these patients, the authors recommend infectious disease consultation to determine the optimal antimicrobial regimen often involving an initial parenteral course of antibiotics followed by a long-term oral regimen. Cure rates in trials involving retention of the implant generally have been disappointing. A recent randomized controlled trial of rifampin in implant salvage among a selected group of patients with joint prosthesis or fracture-fixation device staphylococcal infections yielded promising results.[30] Ongoing studies in OIF/OEF patients will hopefully provide valuable data on how to best manage these complex cases.

Protocol for Management of Infections for Amputee/Extremity Trauma Patients

An axiom for the treatment of soft tissue or hardware infections is debridement of infected or devitalized tissues and removal of implanted hardware. Antibiotics serve a secondary role that is effective only with adequate debridement. Without sufficiently removing the infected source, most antibiotic regimens fail regardless of duration of treatment regimen. Recommendations for optimal duration of therapy vary and no standard consensus guidelines exist.

Treatment of osteomyelitis poses several clinical difficulties. No studies have addressed prospective randomized clinical trials assessing the length of antimicrobial therapy in these patients. In the setting of traumatic injury, osteomyelitis has a heterogeneous disease course and the optimal duration of antimicrobial therapy is unknown. In experimental models, 4 weeks of therapy were more effective in sterilizing the bone than 2 weeks of therapy. Surgical debride-

ment was not part of these models; therefore, shorter courses of therapy may be as effective when paired with extensive surgical debridement.[31] Although it typically takes approximately 6 weeks for vascularized soft tissue to cover the debrided bone and anecdotal experiences suggest a higher relapse rate with shorter durations of therapy, most experts recommend 4 to 6 weeks of parenteral antimicrobial therapy.[32]

A similar problem exists for skin and soft tissue infections. The duration of antibiotics for infections involving only the skin and soft tissue has not been definitively proven. Most experts recommend 7 to 14 days of therapy or until resolution of clinical signs and symptoms. Therefore, each patient should be followed closely to ensure adequate treatment and to prevent the spread of the infection to deeper tissues.

Principles of Management. It is difficult to compare the available literature because no standard case definitions, treatments, or patient populations exist, resulting in large discrepancies among outcomes that may not be based exclusively on treatment methods. In addition, small sample sizes in many studies preclude the ability to make definitive conclusions and the sample populations vary (civilian trauma vs combat injury).

The inoculating event is important in determining management. Posttraumatic osteomyelitis may occur as a direct result of bony injury following trauma or arise from nosocomial infection. Ideally, antibiotic selections are guided by wound culture and sensitivity results. Empiric antibiotic regimens should be chosen based on the medical center's antibiogram (local sensitivities and resistance patterns).

Patients with amputations/extremity trauma often have serial debridements ("washouts") prior to wound closure. Interval surgical exams are important in monitoring for resolution of infection. Findings of new purulence, fluid collections, or necrotic tissue should be cultured because it may represent a new infection or an emerging resistant organism. Cultures should not be taken during serial washouts if no evidence of infection exists because positive culture results may represent colonization.

Quantitative operative cultures may be used as a marker of decreased or resolving bacterial burden. Quantitative culture requires weighing and careful preparation of the specimen for serial dilutions to determine whether the colony count is greater than 10^5 colony-forming units per gram of tissue. Colony counts of this magnitude are correlated with a greater likelihood of infection associated with wound closure. Direct Gram smears of known quantities of specimen can be used to give an immediate assessment of organism load. Because quantitative cultures are time consuming and labor intensive, not all laboratories have procedures for performing these assays. The authors therefore recommend against performing such cultures.[33]

Different inflammatory markers can be used to monitor infection, but none have been studied in the authors' particular patient population. These markers include C-reactive protein, erythrocyte sedimentation rate, and pro-calcitonin level. Unfortunately, these markers differ based on the specific patient's inflammatory response to the initial trauma, surgical trauma, and underlying comorbidities. The most important concept in monitoring these parameters is the observance of trends. A significant increase in any of these serum studies may prompt further radiologic or surgical exploration for unresolved infection.

Orthopaedic consultants often obtain serial plain radiographs. Although plain films are insensitive for monitoring osteomyelitis, findings of osteopenia and thinning of cortical bone or sequestra should prompt closer monitoring or cross-sectional imaging studies. Serial cross-sectional imaging studies (computed tomography [CT], magnetic resonance imaging, etc) may be used, but they are significantly more expensive and patient transport may present challenges. To further complicate imaging study of osteomyelitis, noninfectious postoperative scarring or edema in traumatized bone can persist for up to 1 year.[34] Heterotopic ossification (HO) has also been commonly seen in the OIF/OEF population; however, it does not appear to pose an increased risk of infection.[35]

Infection Control and Surveillance in Returning Warriors

The emergence of MDROs is a worldwide dilemma and adds to the complexity of care for wounded and ill service members returning from theater. The predominant and troublesome MDRO that military personnel face returning from OIF/OEF is ABC.[9,10,12,13] Several reports have focused on the ABC outbreak that appears to be related to contamination in field hospitals.[13] *Acinetobacter* has been appreciated since the Vietnam War and it continues to be a significant problem for personnel returning from OIF/OEF.[36]

Other MDROs of concern in major military hospitals and in civilian hospitals are gram-negative organisms, *Klebsiella pneumoniae*, *P aeruginosa*, vancomycin-resistant enterococcus, and ESBL-producing organisms. These MDROs have a predilection for transmission in healthcare facilities and persist unless diligent control and containment measures are undertaken. Wounded service members, particularly those with open nonhealing wounds or burns, are at risk for bacterial colonization and/or infection. Treating these infections

with broad-spectrum antimicrobials leads to depletion of normal gut flora, increasing the risk for *Clostridium difficile*-associated disease.

Measures for successful control of MDROs, which have been documented in the United States and abroad, consist of a variety of combined interventions.[14] These interventions include hand hygiene by all healthcare providers, the use of active surveillance cultures for MDRO colonization, contact precautions, infectious control education, enhanced environmental cleaning, and improvements in communication between healthcare providers/facilities about patients with MDRO infections. Each of these measures should be customized for application within each healthcare facility and the local community under the guidance of an active and informed infection control committee of specialists in infectious disease, occupational health, preventative medicine, pharmacy, and clinical laboratory services. However, it is the responsibility of individual healthcare providers to play an active role in the successful elimination of MDROs in their patients, their hospital, and their community.

Initiation and Surveillance of Contact Precautions

Active surveillance of MDROs, particularly with MRSA, is being widely conducted in the United States. In 2003 major military medical treatment facilities began surveillance cultures of groin and axillae for ABC and nares for MRSA on all soldiers directly admitted from theater. Population and need determines targeted surveillance. Contact precautions are used as a containment measure before MDRO isolation from culture when there is a high suspicion for infection (eg, on hospital admission and/or in patients with open draining wounds not contained in a dressing). Methods for determining colonization are not standardized among institutions. CDC guidelines should be used as a reference when making decisions regarding colonization surveillance methods.[14] Any healthcare provider can initiate contact precautions, but they should be removed in conjunction with infection control practitioners and hospital policy.

CDC defines contact precautions as the wearing of gown and gloves when in contact with the patient or anything that has touched the patient.[14] Although visitors who touch the patient do not always need to comply with these measures, the rationale for healthcare providers to wear protective gear is to prevent the transmission of bacteria from one patient to another. In some circumstances it is not feasible for each patient to have a private room. In these cases patients with the same MDROs can be located together. At WRAMC family members are required to wear a gown and gloves only if they will come into contact with blood or body fluids. Other institutions require family members to wear a gown, gloves, and masks (when concern for airborne transmission exists) at all times. The efficacy of any of these strategies requires strict adherence.

Discontinuing Contact Precautions

Few data support standardized criteria for removing contact precautions for patients colonized or infected with MDROs. The clearing protocol shown in Table 10-1 is used in two major military medical treatment facilities to clear patients and to reduce their social isolation.[37] Providers should know their patients' status and be involved in a clearing protocol as soon as antibiotic therapy has ceased for 72 hours and wounds are healed.

Environmental Cleaning

The environment plays an increasingly significant role in the transmission of nosocomial MDROs. ABC and MRSA can live for weeks on surfaces, especially "high-touch" surfaces.[38] Daily housecleaning of such surfaces, particularly IV poles and bedrails, is critical. Hospital-grade disinfectants with high kill while drying should be used in patient rooms, especially during patient turnover. Assiduous environmental cleaning by hospital housekeeping staff has been shown to reduce the frequency of vancomycin-resistant enterococcus cross contamination.[39]

Once the colonized patient is discharged and returns for rehabilitation in outpatient clinics, the risk for transmission is decreased but not eliminated. Patients with amputations and other combat-related injuries often require multiple readmissions and clinic visits for rehabilitation. They are continually at risk for acquiring a new infection or spreading their colonized microbes. In WRAMC's outpatient clinics patients with open wounds or undergoing dressing changes must be treated in designated areas. In therapy gyms the healthcare provider monitors and cleans mats and other equipment used by patients with the appropriate germicide.

Hand Hygiene

Hand hygiene remains the cornerstone of infection prevention and control in healthcare and community settings; therefore, hospital administrators should give

it the highest level of attention.[40] Soap and water may be as effective as antimicrobial soap. Alcohol hand gels with moisturizer have been shown to be effective against all organisms except *C difficile* and spores. Hand hygiene for healthcare workers is required before and after any patient care and after removing gloves. Routine surveillance of handwashing is recommended to enforce its importance and identify areas for intervention within an institution.

Communication and Education

Providers communicating to bed control managers, discharge planners, and others have been very successful in alerting others of a patient's MDRO status. Healthcare providers have a critical role in educating patients of the significance of MDRO colonization or infection. To prevent feelings of isolation and anxiety, simple language should be

TABLE 10-1

CLEARING PROTOCOL SUMMARY CHART

To Clear For	When	Obtain These Cultures	Order as	Repeat	Clear
Acinetobacter	Off antibiotics 72 hours, clinically improved, hardware sites clean and dry	Groin, axillae, nasal swabs Original site if sputum, urine, or open/draining wound	Rule out *Acinetobacter* (ACI), choose site from pick list (groin, axilla, nares, wound, sputum, other)	Same cultures two more times, each 72 hours apart	If all cultures are negative and approved by ICES
MRSA	Off antibiotics 72 hours, clinically improved, hardware sites clean and dry	Nares Original site if sputum, urine, or open/draining wound	Rule out MRSA, select nasal swab and other sites from pick list	Same cultures two more times, each 72 hours apart	If all cultures are negative and approved by ICES
VRE	Off antibiotics 72 hours, clinically improved, hardware sites clean and dry	Stool cultures or rectal swab Original site if sputum, urine, or open/draining wound	Rule out VRE, choose sites from pick list	Same cultures two more times, each 72 hours apart	If all cultures are negative and approved by ICES
MDRO/ESBL Gram negs (*Klebsiella, Pseudomonas*)	Off antibiotics 72 hours, clinically improved, hardware sites clean and dry	Urine or peri-anal/rectal swab Original site if sputum, urine, or open/draining wound	Rule out MDRO choose sites from pick list	Same cultures two more times, each 72 hours apart	If all cultures are negative and approved by ICES
Clostridium difficile	Completed 72 hours of treatment	No cultures necessary	NA	NA	If clinically improved and no diarrhea for 24 hours

ESBL: extended spectrum beta-lactamase
ICES: Infection Control and Epidemiology Service
MDRO: multidrug-resistant organism
MRSA: methicillin-resistant *Staphylococcus aureus*
VRE: vancomycin-resistant enterococcus
Initiate clearance cultures when off effective* antibiotics for 72 hours, wounds are healing, hardware is clean, and patient is clinically healing. For long-term patients readmitted, initiate clearance cultures prior to restart of antibiotics.
Do not culture blood, cerebrospinal fluid, or scabbed/healed wounds if these were originally positive.
*Effective antibiotic = one to which the organism is proven susceptible

used to convey the type and significance of infection/colonization to each patient placed on contact precautions.

Fever in the Returning Service Member

Fever in the returning service member should be recognized for its similarities to routine travelers and for its uniqueness related to the combat environment.[9] Rates of disease and nonbattle injury casualties historically exceed battle injuries in most conflicts. Rates have remained high for conflicts within the past decade, although preventive medicine interventions have dramatically reduced the nonpsychiatric and nonbattle injuries. Nevertheless, certain infections should remain high on the physician's differential when treating a returning service member.

Systemic illness, followed closely by diarrheal and respiratory illnesses, constitutes the majority of syndromes in all travelers when studied across six continents.[41] Diarrheal illness is common in deployed personnel with up to 66% of troops reporting diarrhea, but it is an unlikely cause of fever the longer a patient has been back from theater.[9] Physicians should consider more common etiologies of diarrhea and fever (*C difficile*) for patients who have been out of theater for more than 1 week.

Malaria remains a consideration with travel to endemic areas outside the United States. Malaria is a common etiology of fever in the returning traveler, yet it has attack rates of only 10% in most areas of Afghanistan. Malaria from Iraq is rare with few cases directly attributable to travel there.[42] Most of the malaria cases have been caused by *Plasmodium vivax* (80% to 90% in Afghanistan and 95% in Iraq) with the remainder caused by the more life-threatening strain, *Plasmodium falciparum*.[43] Fever secondary to *P vivax* infection, which can occur months after exposure, should be considered as a potential etiology in at-risk patients for up to 1 year after return from deployment.

Q fever, caused by *Coxiella burnetii*, has been diagnosed in returning service members, with more than 30 cases diagnosed during OIF/OEF.[9,44,45] Classically, patients have been exposed to animals, such as cows and sheep, but several of the cases from OIF/OEF did not have known direct exposure. Q fever, which has a variable clinical course, often presents as a nonspecific febrile flu-like illness with pneumonia and/or hepatitis. Chronic infection most commonly involves the heart, and specific recommendations have been developed to monitor for chronic disease.[46]

Leishmaniasis, spread by the sand fly, represents another potential cause of fever in the returning service member. More than 1,200 cases of cutaneous leishmaniasis and four confirmed cases of visceral leishmaniasis have occurred.[47] Cutaneous leishmaniasis is characterized by a nonhealing skin ulcer, without systemic symptoms. Visceral leishmaniasis is a systemic illness that manifests as a syndrome of fever, fatigue, night sweats, weight loss, gastrointestinal upset, hepatosplenomegaly, impaired liver function tests, and pancytopenia. Patient travel to endemic areas will increase one's suspicion of leishmaniasis, and diagnosis can be made with a serologic assay.[9]

Apart from wound-specific infections, service members are at risk for infections transmitted via blood transfusion. Many service members receive massive transfusions (greater than 10 units of blood products). Although screening of the prepared blood supply is adequate, wartime often necessitates the use of field-expedient donors that may not have had recent screening for potentially newly acquired diseases such as human immunodeficiency virus and viral hepatitis. Unlike hepatitis A, which is rarely acquired via transfusion, hepatitis B and hepatitis C are associated with blood transfusions. One study from 1996 estimated nonwar-related transmission rates of 1 per 64,000 units transfused for hepatitis B virus. Hepatitis C virus was estimated to have transmission rates of 1 per 103,000 per donor exposure in the United States. Human immunodeficiency virus transmission rates have been reported at 1 per 493,000 units transfused in the United States.[48] Although rates are not yet known for deployed service members, new infections have been identified in returning OEF/OIF service members.

Providers caring for hospitalized service members who have sustained injuries during a deployment should be aware of all potential causes of infections. Although it is the tendency to focus on the areas of trauma, potential travel-related infections must also be considered. Using the methods discussed in this section and reviewing the infections that are endemic to a deployed area will help the provider make an expedient diagnosis and decrease morbidity.

WOUND CARE MANAGEMENT

Introduction

Wound care management is a critical component of military medicine, especially in the traumatic amputee's care. Combat injuries often require complex wound care at multiple sites throughout the body. Because of the advances in body armor, fewer wounds are being seen to the chest and abdomen than had been reported in prior

wars. Furthermore, given the combination of immobilization, peripheral nerve injuries, and sedating effects of multiple medications, these patients are at even greater risk of developing problems such as pressure ulcers or compressive neuropathies. Therefore, proper positioning of the patient at all times throughout the echelons of care will likely reduce the risk of iatrogenic injuries. Judicious application of a standardized algorithm may reduce morbidity and mortality associated with wound management as well as economic burden.

Although it would seem reasonable that the amount of training a medical professional receives in wound care management would be commensurate with its degree of overall medical significance, this is not the case. Wound care tends to be an area of healthcare where outdated dogma often supersedes current medical knowledge. In addition, it is often mistakenly judged to be a subject, rather than a required dedicated field of medicine within itself.

A provider cannot make competent decisions regarding the "how" of treatment when there is an incomplete understanding of the "why." In this section a focused discussion of the essential principles of wound care will be presented. Unfortunately, a detailed analysis of wound types, their corresponding nomenclature, and specific treatment algorithms is beyond the scope of this section. Therefore, the following review will address normal wound healing, factors that negatively affect outcomes, and general principles to optimize wound healing.

The Phases of Wound Healing

The four stages of wound healing are

1. hemostasis,
2. inflammation,
3. proliferation, and
4. remodeling.

Hemostasis

The hemostatic phase starts when the skin is first broken and stops when blood loss is controlled. The most immediate reaction to vascular injury occurs at the level of the vessel itself that reflexively vasoconstricts when damaged. The two primary means of hemostasis, however, involve initiation of the coagulation cascade and the formation of a platelet plug. These events are elegantly triggered when normally extraluminal materials such as collagen, thrombin, and tissue factor are exposed to the intraluminal milieu. The time required depends on the wound size and intrinsic factors associated with the patient's health.

Inflammation

The inflammatory phase, under normal circumstances, lasts 3 to 5 days and is defined by the presence of neutrophils. The role of the neutrophils in a wound bed is context dependent and under certain conditions it can be disadvantageous. As a member of the body's innate immune response, neutrophils are critical but their actions are nonspecific. Neutrophils act by releasing cytokines and chemokines within the wound bed, leading to free radical production and creating an unfriendly environment for both pathogens, as well as often the body's own tissue-healing cells. Neutrophils also release the enzymes collagenase and elastase into the wound bed to break down the remaining extracellular matrix in preparation for subsequent wound-healing stages. By preventing pathogens from establishing foci and removing the detritus of an injured wound bed (extracellular matrix, dead pathogens, and native cells), an accessible route of entry for the body's incoming regenerative cells is created.

Neutrophils will generally persist until most of the bacteria and necrotic tissue are removed. Neutrophils are vital acutely following injury, but they become a deficit in subsequent healing stages. Wound debridement at this later stage is therefore vital. The transition to the proliferative phase of wound healing is facilitated by manually cleaning a wound bed of bacteria and necrotic tissue. The success of wound debridement depends on proper technique. Excessive force may lead to renewed involvement of the neutrophils and only reinitiate the wound-healing cascade.

Proliferation

Just as the inflammatory phase was defined by the neutrophil, the proliferative phase is defined by the macrophage. Macrophages consume bacteria and nonviable material, and release enzymes to break down the existing extracellular matrix. However, macrophages, which are more sophisticated and multidimensional than neutrophils in their overall function, can be considered the orchestrators of wound healing. The release of growth factors and cytokines leads to the migration of keratinocytes and fibroblasts into the wound bed to initiate reepithelialization and granulation tissue formation, respectively.

Three steps in the proliferative phase include

1. reepithelialization,
2. granulation tissue formation, and
3. wound contraction.

Reepithelialization. The first step in the proliferative phase, reepithelialization begins as early as 24 hours postinjury. When an area of skin is broken, the loss of contact inhibition that occurs between epidermal cells stimulates replication and migration into the wound bed. This migration is coordinated by macrophages.

Granulation Tissue Formation. The second step, the granulation tissue formation, can begin as early as 3 days postinjury and is visually the hallmark of the proliferative phase. The wound bed begins to take on a shiny, reddish-pink, cobblestone appearance. Macroscopically, each red cobblestone represents a burgeoning new capillary, and the shiny texture is imparted by the loose extracellular matrix, which is produced by fibroblasts. When the intricate processes of reepithelialization and granulation tissue formation are not coordinated, they can work in opposition. For example, a wound will stop granulating once it is epithelialized, even if the wound has not yet filled in. Similarly, if epithelialization never occurs, granulation may continue unabated until a heaping mound of granulating tissue towers over the surrounding periwound skin. The etiology and treatment of these conditions will be discussed later in this chapter.

Wound Contraction. The third step in the proliferative phase is wound contraction. When a wound is mature enough, fibroblasts are signaled to alter their gene expression, the synthesis of actin filaments is upregulated, and the fibroblast transforms into a myofibroblast. Myofibroblasts link up across the wound bed and over time pull the wound closed.

Remodeling

The remodeling phase, the final and longest wound-healing phase, frequently lasts more than 2 years. It is largely mediated by fibroblasts and consists primarily of collagen deposition along the lines of stress. Remodeling is a dynamic process and increases the tensile strength of the wound where it needs it most.

Abnormal Wound Healing

Abnormal wound healing occurs when a chronic wound fails to proceed through the aforementioned phases, resulting in a wound that is deficient in its anatomic and/or functional integrity. Wound healing is simplified and described in phases; however, it is a continuum involving countless cells, cytokines, and yet to be identified factors. A wound can be further complicated by extrinsic factors, such as infection, or intrinsic factors specific to the patient such as malnutrition or defined genetic-dependent characteristics. The wound-healing mechanisms are overwhelmed, and intervention is required to facilitate recovery. The differential diagnosis for a nonhealing wound is relatively narrow and for the vast majority of cases will be related to at least one of the following intrinsic or extrinsic factors. Intrinsic factors may include chronic inflammation, excessive granulation or insufficient epithelialization, excessive fluid (maceration) within the wound bed, poor nutritional status, etc. Extrinsic factors may include insufficient or excessive debridement and/or inadequate infection management.

Chronic Inflammation

Chronic inflammation in the presence of infection, for example, is an appropriate and necessary bodily response. The appropriate clinical action in this situation would clearly be to treat the infection and not the inflammation. Conversely, if a wound appears persistently inflamed yet not infected, other etiologies must be sought.

Insufficient versus Excessive Debridement

Aside from infection, the most likely causes for persistent inflammation within the wound come from repeated trauma or necrotic tissue. As discussed previously, fixing one issue can often exacerbate the other. To clear a wound of its necrotic tissue, for example, the wound must be debrided. An aggressive debriding schedule, such as wet-to-dry dressing changes every 4 hours, may cause excessive trauma and a situation of diminishing returns. Likewise, in an exudative or otherwise wet wound, applied dressings are unable to dry and therefore debridement would not be accomplished with subsequent removal. Wounds with substantial eschar may require sharp debridement, whereas wounds with less eschar may respond to autolytic or enzymatic debridement. The clinician should choose the most appropriate means of debridement depending on the wound characteristics.

Granulation versus Epithelialization

Complications associated with granulation are often compounded with problems of epithelialization. Specifically, a hypogranulating wound often localizes the problem to the wound bed. Conversely, a hypergranulating wound often indicates a problem with epithelialization (ie, the periwound skin).

Consider the following: A wound bed is chronically inflamed from necrotic tissue. The surrounding skin, however, is supple and healthy. Because of the persistent inflammation, the wound bed granulates at

a very slow pace, but the surrounding skin continues to migrate in at a normal pace. As a result, the edges of the wound margins are opposed over an insufficient wound bed.

Consider a wound that has a very healthy wound base, but has persistently macerated wound edges. The wound will granulate at a normal pace but the wound margins will fail to oppose secondary to insufficient epithelialization. The granulating tissue, with no signal to stop, will therefore grow unabated, rising above the level of the surrounding skin. This would be referred to as a hypergranulating wound, although a more accurate characterization would be a "hypo-epithelializing" wound.

A wound may fail to epithelialize properly for several reasons. One reason is the rolled edge or epiboly. Under normal circumstances, periwound skin divides and migrates down into the wound bed. Occasionally, however, these cells can become misdirected and like the crest of a breaking wave curl up underneath themselves. Because of contact inhibition, the cells stop dividing and epithelialization fails. A close inspection of the wound can identify this phenomenon. Sharp debridement is usually the quickest and most effective solution. The remaining reasons for insufficient epithelialization are simply related to unhealthy periwound skin, the most common etiologies being a macerated wound edge, unrelieved pressure, persistent inflammation, or infection.

A slowly granulating wound—more often than not—indicates an unhealthy wound base. Desiccation, persistent inflammation, infection, a cold wound bed, and tightly packed gauze are all common causes. Whatever the etiology, it is critical to remember that if epithelialization has already occurred, the wound bed will not granulate even if the underlying problem is corrected. It is therefore occasionally necessary to cauterize the surrounding wound edges with silver nitrate to prevent epithelialization while the wound bed recovers.

Desiccation versus Maceration

The task of balancing optimal moisture levels between wound and skin is often the most challenging aspect of wound care. Depending on age, sex, and body fat, the amount of water in human bodies ranges from 50% to 70%. Moisture is essential for wound healing. Without moisture, migrating cells and chemical signals have no medium in which to travel, and the viability of enzymes and growth factors cannot be maintained.

Although humans need water, they are unable to live in it. The keratinized stratum corneum of human epidermis keeps excess moisture from penetrating to deeper levels; however, this attribute is negated with an open wound. Once upper stratum corneum and basilar layers are interrupted, epidermal cells become exposed to a hypotonic solution and will gradually swell and burst. The desmosomes that anchor the epidermal cells to the dermis and to each other will eventually become disrupted, and the wound will become larger.

A skilled wound care specialist will consider the periwound skin as part of the wound environment because it is from this healthy rim of tissue that most of the regenerative epithelial cells originate. Management of the periwound fluid balance is critical. Through the judicious use of dressings, emollients, and barriers, the wound bed may be kept moist without causing maceration of the wound margin. Likewise, the wound must be kept dry enough without causing desiccation of the wound bed.

Infection versus Antibiotics

By definition a wound is infected when the bacterial load exceeds 100,000 organisms per gram. A clinical diagnosis may be made based on signs and symptoms of infection to include purulence, erythema, or evidence of advancing cellulites. As discussed in the previous section, determination of colonization versus active infection is critical in determining appropriateness of antibiotic management. Additional signs and symptoms of infection include

- induration,
- pain,
- fever,
- changes in color,
- persistently foul odor,
- increased drainage,
- friable granulation tissue that easily bleeds, and
- delayed healing.

The indiscriminate use of topical antibiotics has led to bacterial resistance and the alteration of normal skin flora. In addition, the nonselective nature of these antibiotics also causes damage to native cells. Some bactericidal agents such as hydrogen peroxide and iodine are more toxic to human cells than to bacteria. These characteristics warrant judicious use of topical agents in wound management.

Impaired Healing Response

Thus far, the discussion of abnormal wound healing has revolved around direct extrinsic factors, but an equally important aspect is the health of the

wound-healing machinery itself. If a patient's system is already stressed from sepsis, for example, the body simply cannot allocate the resources necessary for wound healing. Broadly speaking (and with some overlap) there are five main categories of problems that can cause an impaired healing response:

1. a diseased state,
2. an impaired immune system,
3. malnutrition,
4. toxins, and
5. medications.

In the inpatient setting special attention should be paid to the patient's nutritional status and medication profile. Immunosuppressants such as corticosteroids and nonsteroidal antiinflammatory medications (NSAIDs) are frequent culprits. Cytotoxic topical agents as discussed above can also slow things down considerably. For a patient whose nutritional status is compromised, weekly prealbumin levels are indicated and a certified nutritionist should be involved as early as possible. Tobacco use also can seriously retard wound healing. Patients must be educated about this and offered a tobacco cessation program. This is an especially important point among traumatic amputees whose wounds have a tenuous blood supply and associated tissue viability; the success of limb preservation depends on optimizing the wound environment.

Wound Treatment

Thousands of wound care products are available and likely an equal number of institution-specific treatment algorithms. To the uninitiated, this abundance of choice can spuriously equate with degree of complexity. Developing expertise in wound care takes years of hands-on experience. Basic proficiency depends on pattern recognition and determining the why, when, and how of the main interventions.

Debridement

Debridement attempts to remove all unwanted elements from a wound such as eschar, slough, fibrin, pus, and bacteria. Because of their common yellow color slough, fibrin and pus are occasionally confused. Slough is loosely adherent, partially solubilized dead tissue that can be stringy or soupy in its texture and usually lacks a persistent foul odor. Fibrin is a very adherent, almost rubbery substance that is formed as a result of fibrinogen leaking into the inflamed wound bed. Pus, which has a milky texture, is usually accompanied by other signs of infection and ominously indicates the presence of purulent organisms.

So why debride? The most direct answer is that by not debriding a patient is at increased risk for infection, impaired wound healing, and potentially further surgical revisions. For an amputee this may have a significant impact on his or her functional capabilities if this revision leads to a shorter residual limb. An undebrided wound cannot be properly visualized and therefore cannot be properly assessed. What may initially look like a partial thickness wound, for example, could be deep enough to involve both muscle and bone and could be obscuring a deep infection. In addition, nonviable tissue takes up space and acts as a barrier against further cell entry. In this way, regenerative cells are thwarted from repopulating the wound bed and immune cells are denied access to the growing number of bacteria in the eschar and slough. Chronic inflammation results when nonviable tissue causes persistent neutrophil accumulation that may prohibit cellular progression to granulation and reepithelialization. Debridement is a necessary and powerful tool that can rapidly effect change in a relatively short period.

There are four main techniques to debride a wound:

1. sharp,
2. autolytic,
3. enzymatic, and
4. mechanical.

Sharp Debridement. Sharp debridement involves the use of a cutting instrument, such as a scalpel or scissors, and can be performed at the bedside by qualified personnel. It is the most rapid—and often the most effective—method of debridement. Large wounds that are completely covered in adherent fibrin or eschar are prime candidates for sharp debridement, and depending on patient tolerance may occasionally require more than one session to complete the bulk of the debriding process. The ultimate goal is to expose a healthy pink tissue base, remove all barriers to granulation, and ensure accurate staging and assessment.

Autolytic and Enzymatic Debridement. If a wound contains more than a mild to moderate amount of debris, sharp debridement is usually a necessary initial intervention. After the bulk of necrotic tissue is removed, however, the need for continued debridement must be weighed against the tradeoffs of excessive tissue handling, trauma, and risk of contamination. Under these circumstances and when the wound is otherwise healthy and uninfected, autolytic debridement (with or without exogenous enzymatic debridement) becomes ideal.

Autolytic debridement relies on the body's endogenous enzymes and phagocytes. Toward this end, an occlusive dressing is used that is usually changed no sooner than 72 hours. The occlusive dressing provides a warm, moist, and unperturbed environment that is ideal for wound healing. Because the dressing is not changed multiple times per day, the body's enzymes accumulate in the wound and break down nonviable tissue. To augment this process, exogenous enzymes, such as collagenase, papain, and urea, are occasionally applied to the wound bed. When the dressing is finally changed, much of the debris has become loosened and is easily removed with limited patient discomfort.

Because this method of debridement relies on occlusion, however, presence of active infection is a contraindication to use of this technique. In addition, those that change the dressing should be aware that it is not uncommon for occlusive dressings to have a strong odor. In contrast to infected wounds, however, the odor will not persist once the wound is cleaned.

Mechanical Debridement. Although inferior to sharp debridement at removing recalcitrant fibrin or eschar, mechanical debridement can be a very effective and appropriate means of removing less adherent necrotic tissue from a wound. In addition, most forms of mechanical debridement can be performed with relatively little training. Examples include simple manual scrubbing with gauze, irrigation with pulsatile lavage, and wet-to-dry dressings. The drawback of mechanical debridement is that it nonselectively removes both viable and necrotic tissue from a wound bed. Judicious use of this technique is required.

Wet-to-dry dressing is often a first-line treatment in wound management. However, it may not be appropriate in every clinical situation. In light of the biomechanics of wound healing, this technique may be deleterious to wound healing. The recurrent trauma to the wound bed beyond that necessary for adequate debridement of nonviable tissue may further complicate wound management.

The technique necessary for successful use of wet-to-dry dressings depends on the dressing changes every 12 hours. This frequent inspection of the wound leads to significantly more wound exposure than when using an occlusive dressing, causing inflammation and increasing the risk for contamination. In addition, regular cotton gauze sheds particulate matter when allowed to dry into a wound bed, which can be another source of irritation and inflammation. Wet-to-dry management of wounds is one of the more painful and (additively) time-intensive debridement methods. One benefit of using wet-to-dry dressings is the ability to perform frequent wound inspections particularly between surgical washouts. The disadvantage is the increased risk of excessive moisture leading to maceration of the surrounding skin, with inadequate drying thereby losing the debridement function. Debriding occurs as the adherent gauze is removed from the wound; if the gauze is unable to dry (or, alternatively, if it is remoistened before removal), no debriding occurs.

Another critical point (and this applies to all dressings) is that wounds should not be "packed," but instead they should be "filled." Gauze should be trimmed to an appropriate size, and the wound should be gently filled with the material. Tightly pushing an oversize dressing into the wound or "packing" leads to impaired wound healing. A tightly packed wound creates a pressure gradient that impedes the migration of regenerative cells and prevents adequate perfusion of the wound bed. Furthermore, untrimmed gauze may protrude from the wound bed and macerate the surrounding skin.

When Not To Debride

Although a discussion of specific wound types and their management is beyond the scope of this section, there are a few contraindications to debridement.

- Dry Gangrene: Dry gangrene occurs as a consequence of arterial insufficiency and the wound is poorly perfused. The necrotic tissue under these circumstances is actually protecting the wound underneath from infection. Once this barrier is broken, bacteria can more freely penetrate into the wound bed and cause resistant infection.
- Stable Heel Ulcers: Stable heel ulcers do not need to be debrided and should be left alone.
- Pyoderma Gangrenosum: The pathophysiology of pyoderma gangrenosum is linked to immune system dysregulation, although its specific mechanism remains incompletely understood. An apparently small ulceration can become significantly more problematic following debridement.

Restoring Moisture Balance

The majority of dressings and products fall into one of two major categories: (1) those that wet and (2) those that dry. Moisture balance of the wound bed and surrounding margin is critical and often the greatest challenge when treating a wound.

A wound can be thought of as two populations of cells living side by side, each requiring an environment that is toxic to its neighbor. As previously noted, erring too much on the side of moisture for the sake of the wound bed causes the surrounding skin to become macerated and the wound to ultimately grow. Erring too much on the side of dryness for the sake of the surrounding skin causes the wound bed to become desiccated and prematurely arrests the healing process.

The strategy used to obtain balance depends on the character of the wound. A venous stasis ulcer, for example, is notoriously weepy, such that all efforts are aimed at controlling drainage. Because of the failure of venous return, the wound bed of a venous stasis ulcer is essentially supplied with its own "ground water" making it virtually impossible to dry out. Although wound bed desiccation is unlikely, periwound maceration is a major concern. Barrier creams applied to the periwound skin can help protect against maceration but drainage control is critical. If conventional moisture wicking products such as alginates and hydrofibers fail to be effective, tampons are sometimes used with good results. If all wicking measures fail, the frequency of dressing changes must be increased until the periwound skin is adequately protected.

In contrast to venous ulcers, ulcers caused by arterial insufficiency require the opposite approach. Under these circumstances, venous outflow is not the underlying problem, but rather arterial inflow. Without a healthy blood supply to the skin, the wound bed is easily desiccated and needs to be moistened with products such as hydrogels or impregnated gauze. Barring overzealous hydration, periwound maceration is rarely an issue in this situation.

Similar strategies are used for wounds in between these extremes but to a more graded and balanced degree. For a wound that is producing a modest amount of exudate, for example, highly absorbent materials such as tampons or supersponges should be avoided because they excessively dry out the wound bed. Regardless of the initial strategy, the key is frequent inspection with each dressing change and modifications as the wound matures.

DEEP VENOUS THROMBOSIS AND PULMONARY EMBOLISM

Introduction

Despite advancements in prophylaxis and treatment, deep venous thrombosis (DVT) remains a serious complication in combat casualties with polytrauma and amputation. Consequences of DVT include prolonged hospital stay, delay in rehabilitation, secondary thrombophlebitis, or death from secondary pulmonary embolism. The incidence of DVT in trauma patients without prophylaxis has been estimated at 10% to 65%.[49–52] This variability of incidence rates is likely related to the variety of injury patterns seen in polytrauma and combat amputees. Previous reports have demonstrated that patients with spinal cord injuries (SCIs) have the highest rate of DVT among trauma patients.[53]

Although, in general, prophylaxis greatly reduces the risk of DVT, the choice and method of prophylaxis remain complex, especially in polytrauma and combat amputees.[54–58] Current methods of prophylaxis include adjusted doses of oral warfarin, fixed doses of low molecular weight heparin, subcutaneous heparin, aspirin, TED hose (Tyco Healthcare/Kendall Products, Mansfield, Mass), and sequential compressive devices (SCDs). Each of these methods except TED hose/SCDs carries an increased bleeding risk that presents a particular problem to trauma patients, especially those who require frequent returns to the operating room.[59] The use of TED hose and SCDs in trauma patients—especially those with orthopaedic injuries and amputations—is limited when fractures or wounds involve the extremities. Prevention is the best treatment because the medical therapies to treat venous thromboembolic events are controversial and may have associated risk and complications. DVT/pulmonary embolisms are a severe and life-threatening complication of injury.

Risk factors for DVT include

- immobilization,
- trauma,
- malignancy,
- abnormal coagulation factors,
- obesity,
- estrogen therapy,
- advanced age, and
- prior history of DVT.[60–63]

Given the nature of combat injuries and the (often) lengthy evacuation process required to transport these injured service members through increasing echelons of care, it would appear that this patient population would be at even greater risk for developing venous thromboembolic events.

Incidence and Diagnosis from the Walter Reed Experience

Experience in caring for returning combat amputees from OEF/OIF at WRAMC have shown thrombosis diagnosed in about 30%, with about 60% being DVTs

and 40% being pulmonary embolisms. Twenty percent of DVTs were in the arms and 40% were in the leg. The location of the amputation has not been shown to correlate with the location of thromboembolism. The number of days of missed anticoagulation medications did not correlate with clot formation. The number of trips to the operating room correlated highly with clot formation, with more trips to the operating room correlating to a higher incidence of clots. Patients who had a planned trip to the operating room would have medical prophylaxis held the night before and the morning of surgery. In a population of patients undergoing surgery every other day or every third day, the number of days off medical prophylaxis quickly increases. In combination with other accepted prothrombotic factors, including venous stasis, hypercoagulability, and injury to the vascular endothelium, these patients are at increased risk of thrombosis development. Combat amputees with concomitant fracture are more likely to develop a venous thromboembolism (VTE). Comorbid traumatic brain injury (TBI) doubled the likelihood of being diagnosed with a VTE.

For the diagnosis of VTE, computed tomography (CT) was the best screening method for pulmonary embolisms with 100% sensitivity and specificity. The next best screening method was ultrasound, followed by angiography. However, for DVTs, CT scan had 100% sensitivity and 80% specificity, whereas ultrasound demonstrated 100% sensitivity and 91% specificity and angiography was the least sensitive for DVTs. In this young, relatively healthy patient population, physical symptoms of DVT are often vague and rarely readily apparent. Therefore, medical vigilance is critical and providers should have a low threshold for routine screening.

Physical Prophylaxis

Polytrauma and combat amputees are often unable to wear TED hose and SCDs because of their extremity injuries. From the authors' experience at WRAMC, patients able to wear TEDs were less likely to develop a thrombus. A larger number of patients used SCDs, but this higher number may be deceiving. Although the treating physicians order many devices, in practice, patients do not tolerate them or wear them for much of the day and at night. This magnifies the importance of medical prophylaxis.

Medical Prophylaxis

Medical prophylaxis in this population remains debatable. Lovenox (Sanofi-aventis US, Bridgewater, NJ), a low molecular-weight heparin, tends to be the preferred agent within this population because of the ease in stopping and restarting for procedures. It is also simple to convert from prophylactic dosing to therapeutic dosing. Within the monitored setting of the intensive care units, heparin is often used, in part because of the reversibility of its action with protamine.

Minimizing Immobilization

The air evacuation process also must be considered. Antecedent trauma or surgery followed by prolonged air evacuation may be related to the development of VTE in more than half of those service members evacuated from deployments to the Middle East. Any injured patient who must travel via air evacuation faces several flights lasting approximately 6 hours each and additional ground transport time and other transport time to the evacuation sites. This long period of transportation immobilization should lead the provider to evaluate the need for earlier initiation of medical prophylaxis, although risk of bleeding complications must also be considered. The recognition of complications associated with severe polytrauma and combat wound-related amputations requires careful consideration before initiating anticoagulation and should be made on a case-by-case basis. Upon arrival to a tertiary care hospital (level 4 or 5 echelon), every effort should be given to facilitate early patient mobilization. This may include simple passive range of motion of the extremities for the patient restricted to bed or early transfers and ambulation, whether by wheelchair or other assistive device. Although no clear evidence indicates when medical prophylaxis should be discontinued, it is generally considered necessary to continue it until significant independent mobility is achieved.

WEIGHT-BEARING PROGRESSION

Amputations sustained from high-energy combat trauma generally produce significant comorbidity.[64] Femoral and pelvic fractures with coexisting lower extremity amputation present a significant rehabilitation challenge. These complex fractures must be given an appropriate amount of time protected from large distracted forces to allow proper healing. Operationally this is accomplished by implementing various degrees of weight-bearing restrictions that must be balanced with the well-known negative physical and psychological consequences of bed rest and inactivity.[65–68] Unfortunately, little standardized information exists to guide the temporal parameters and advancement of weight-bearing restrictions.

Because of advances in military medicine, timely and thorough evaluations of the musculoskeletal system are

standard. This generally includes aggressive orthopaedic surgical reduction and fixation as part of fracture management. After initial surgical management, fractures progress through a standard sequence of healing that includes inflammation, repair, and remodeling.[69,70] Initial injury characteristics greatly affect the process. In particular, damage to the blood supply and soft tissue is common and lengthens the course of healing.

Generally the orthopaedic surgeon establishes a guide to the rehabilitation team on a patient's weight-bearing status. Therefore, an individual's weight-bearing status should not be advanced without the surgeon's direct consultation. The determination of weight-bearing tolerance and internal fracture stability, which is multifactorial, includes fracture location, type, apposition of fracture fragments, method of fracture fixation, severity of soft tissue damage, blood supply integrity, nutritional status, and associated injuries. Given the numerous patient-specific variables, no standard guidelines are available for return to full weight bearing.

Existing evidence indicates that fracture healing is optimized through loading of the repair tissue and decreased loading negatively impacts healing time.[71,72] Furthermore, evidence exists that even immediate controlled loading may promote healing.[71,73–78] In the rehabilitation setting, controlled loading is accomplished through the use of tilt tables, parallel bars, and aquatic therapy.[79] Care must be taken to prevent excessive, distracting motion and development of pseudoarthroses or nonunion. Serial radiography to assess evidence of healing (and evidence of nonunion) is recommended. Frequent reassessment of patient symptomatology should be undertaken with particular emphasis on the quality of pain. Changes in quality should prompt further evaluation. The interdisciplinary team of rehabilitation professionals and an orthopedist is critical to ensure successful functional return.

Energy requirements are highest during the first two phases of bone healing, where the need for aggressive early nutritional support is critical.[80–82] Caloric, protein, vitamin C, and vitamin D supplementation are required to meet the anabolic demand of wound healing.[82] The presence of electronegativity at fracture sites has lead to the use of bone stimulators to expedite healing.[83–85] Numerous case reports support their implementation in cases complicated by delayed bone union and nonhealing.[83,86–89] Similarly, ultrasound offers a safe, noninvasive modality that may promote fracture healing.[90–93] Yet, rigid research evidence is still lacking to determine the treatment characteristics of bone stimulation.

During the healing process, the sequelae of combat trauma must be actively managed to promote healing and early functional return. This includes decreasing the metabolic demand of infections and open wounds. TBI, which has a high prevalence in the polytrauma patient, presents numerous barriers including its association with HO development.[94–96] The standard treatments for HO rely on the use of bisphosphonates and NSAIDs. These two pharmacological classes should be avoided with concomitant fractures because of their negative impact on healing. Similarly, nicotine intake should be actively discouraged given its inhibition of fracture healing.[97,98]

In the rehabilitation of the combat-acquired amputation novel plans and individualized recovery trajectories are required. Coexisting lower extremity fractures should be closely followed for appropriate healing and management of potential negative sequelae. The return of full weight bearing and ambulatory function depends on a series of patient-specific variables and ultimately it is decided by collective clinical judgment. Rapid advancement of stable fractures and close multidisciplinary monitoring are preferred in contrast to long periods of inactivity.

HETEROTOPIC OSSIFICATION

Introduction

Among recent military amputees returning from combat in Iraq and Afghanistan, a high rate of HO has been seen in amputated residual limbs.[99] HO is the abnormal formation of bone in soft tissues (Figure 10-1). HO develops when pluripotent mesenchymal cells are inappropriately transformed into osteoblasts that contribute to bone production.[100] The precise cause for this transformation in pluripotent cells is unknown.[100] HO is commonly seen and has been well documented in the setting of SCIs, TBIs, burns, after total joint replacements (especially hips), and with severe soft tissue damage. Before the current military conflict there were few HO reports in amputees' residual limbs.

Bone formation in amputees' residual limbs presents numerous rehabilitation challenges. Bone formed in soft tissues of a weight-bearing limb can result in high-pressure areas, creating a risk for skin breakdown. Skin breakdown can have devastating effects on rehabilitation because it often requires prolonged periods of nonweight bearing and presents a risk for infection. In addition, HO in residual

limbs can result in complex residual limb shapes and multiple pressure-sensitive areas that can make prosthesis fitting difficult or impossible. Increased pain, limitations in range of motion, and limitations in ambulation are also complications from HO in residual limbs.

Current diagnosis methods are acceptable. Patients often report changes in pain characteristics, range of motion restrictions, warmth, and socket fitting in their residual limbs. HO is diagnosed by plain radiograph, CT, magnetic resonance imaging, and/or triple phase bone scan. Blood studies such as alkaline phosphatase may also be followed throughout HO development and correlated to bone formation, maturity, and ultimately quiescence.

Current HO treatment methods are less than optimal. Prophylactic measures, which have shown some efficacy, include NSAIDs, bisphosphonates, and/or radiation therapy.[101–105] Once mature, however, treatment of symptomatic HO is limited to surgical resection.

Historical Perspective on Heterotopic Ossification in the Combat Amputee

A thorough literature review reveals few studies describing HO in combat-related traumatic amputees. Those studies are single case reports that demonstrate HO occurring in the amputees' residual limb.[106,107] Prior reports of combat casualties from the Civil War and World War I do not suggest a significant association with HO formation and traumatic amputation.[108–110] A report by Colonel (Retired) Paul Brown, looking at 88 residual limbs in Vietnam combat amputees, reported only 4 limbs (0.5%) as having "bone spur formation" that required surgical excision.[111] Furthermore, Lieutenant General (Retired) Alcide LaNoue, who was chief of orthopaedics at Valley Forge General Hospital in Pennsylvania, reported seeing only a "few cases of ectopic bone in residual limbs" in more than 410 amputations that were treated under his command during Vietnam.[112]

Heterotopic Ossification from the Walter Reed Experience

WRAMC saw a greater than 50% incidence of HO formation in combat amputees returning from OEF/OIF. This is consistent with an estimated 62% incidence noted by Potter et al in a 2006 observational review of a similar patient population.[113]

It is, therefore, important to determine how the identified risk factors from this patient population might differ from those of prior conflicts. Service members with traumatic amputation from the Vietnam War had injuries complicated by retained metal fragments, other fractures, wound infections, and skin grafts.[111] Some factors that do appear to differ from past populations are

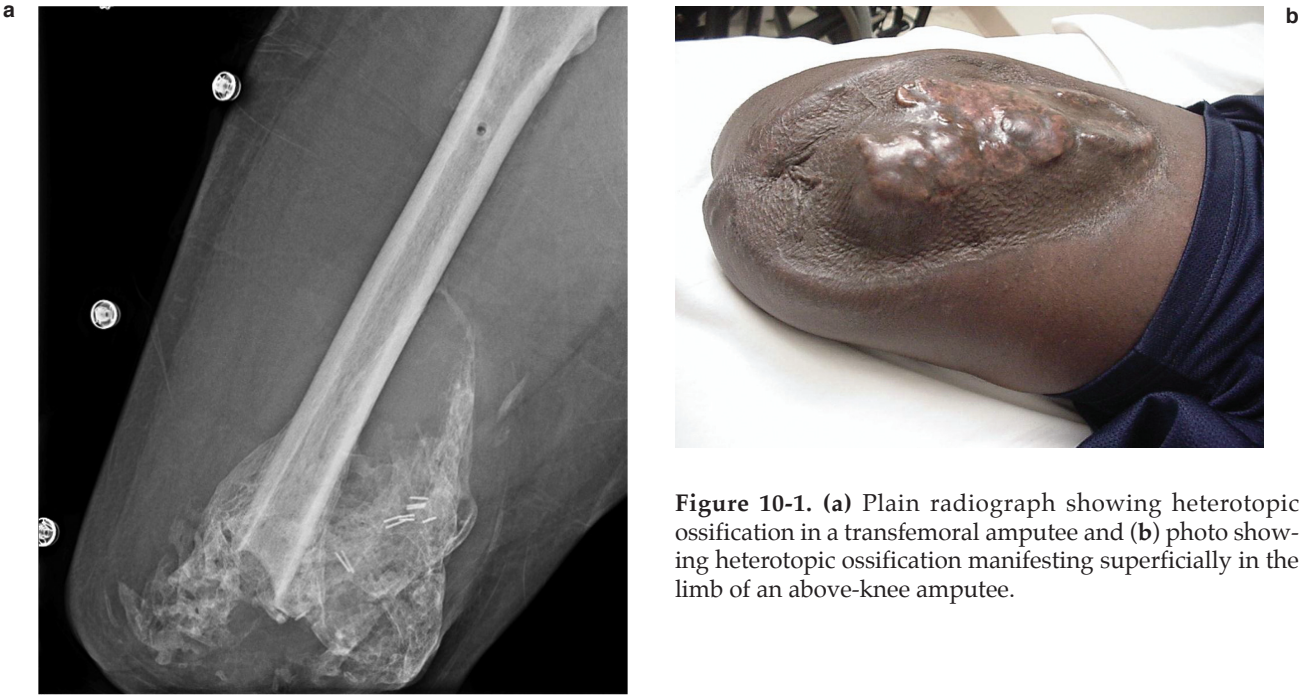

Figure 10-1. (a) Plain radiograph showing heterotopic ossification in a transfemoral amputee and (**b**) photo showing heterotopic ossification manifesting superficially in the limb of an above-knee amputee.

- causative pathogens of wound infections,
- overall increased severity of secondary injuries,
- increased incidence of brain injuries,
- increased numbers, and
- types of surgical procedures/debridements.

One major differentiating factor is modern technology and training of initial responders (ie, the combat medic). Advances in forward care and prompt aeromedical evacuation with better technology in combat personal protective gear have allowed service members to survive injuries that would have been fatal in the past. This has intensified the incidence, type, and severity of secondary injuries and complications. Wound care in the highly advanced surgical arena has changed significantly over the past 40 years. The majority of Vietnam amputees received at Valley Forge General Hospital had open residual limbs, which were debrided with wet-to-dry dressings and rarely required more than one revision.[111] In the current conflict with its emphasis on limb preservation and rapid movement of injured personnel through ascending echelons of care, service members are presenting to continental US tertiary care centers with increased severity of wounds, secondary injuries, and antibiotic-resistant wound infections that necessitate an increased number and complexity of surgical interventions.

Surgical advances such as pulsed lavage debridement and vacuum-assisted wound closure have revolutionized soft tissue injury management and allowed a higher percentage of successful limb preservation attempts. However, the emphasis on limb preservation, which starts at wound triage, leads to tissue preservation with micro- and macro-trauma. This traumatized tissue, which most likely would have been removed in a similarly injured Vietnam War service member, may contribute to the triggering mechanism of cellular differentiation and HO formation.

Another contributing factor is the type and severity of wound infections. Modern weaponry coupled with nontraditional projectiles such as the types of material used in improvised explosive devices appear to cause more contaminated and fragmented wounds. This has contributed to the increased quantity of wound infections and the increased virulence of microorganisms. Approximately 75% of amputee patients with HO at WRAMC had a wound infection. *Acinetobacter baumanni* was the responsible microorganism in half of those infected. Before OIF/OEF *A baumanni* was primarily a hospital-acquired infection and not a common cause of wound infection. Prior studies have also shown *A baumanni* to be more difficult to treat because of increased antimicrobial resistance.[114] The authors' experience in treating this microorganism is consistent with these findings. Patient infection secondary to this pathogen often required multiple weeks of intravenous antibiotics and multiple wound debridements. Wounds infected with *A baumanni* significantly increased the risk of HO development; however, the mechanism is unclear. HO development may be attributed to factors associated with the bacteria, but the etiology of HO is most likely multifactorial and includes factors intrinsic to the patient. HO development warrants further study.

A comorbidity of TBI was found to have the greatest correlation with HO development. Nearly 40% of the WRAMC OEF/OIF patient population had some degree of brain injury. This incidence is markedly increased compared to the 12% to 14% reported from the Vietnam War.[111] The increased incidence attributed to decreased mortality from brain injury is secondary to technological advances and acute management. Mortality from brain injuries among US combatants in Vietnam was reported at 75% or greater.[115] Studies show that brain injury alone can cause HO in 15% to 40% of patients.[116] Studies also suggest that having a brain injury in combination with structural trauma has an additive effect on HO frequency.[116]

The decisions to use prophylactic medications by the primary medical teams were determined largely by extrapolating evidence from other disorders. An abundance of evidence supports the efficacy of multiple types of NSAIDs to prevent HO, especially involving traumatic injuries.[117] Banovac et al[118] showed treatment with the cyclooxygenase (COX)-2 inhibitor, Rofecoxib, to be clinically significant in preventing HO in patients with SCI. The advantage of a COX-2 inhibitor versus a traditional NSAID is based on the gastrointestinal protective properties of the COX-2 inhibitors. It is believed that these medications inhibit prostaglandin synthesis and thus reduce the inflammation and proliferation of mesenchymal cells.[119] Etidronate is in the class of medications known as bisphosphonates. Numerous studies show its efficacy in preventing HO in SCIs and TBIs.[120,121] However, some studies have demonstrated HO recurrence with treatment cessation.[122] Etidronate is thought to decrease HO formation by inhibiting the conversion of amorphous calcium phosphate compounds into hydroxyapatite crystals, which is one of the final steps in bone formation.[123]

Radionuclide bone imaging roentgenographic studies have shown that the onset of HO—regardless of etiology—ranges from 3 to 12 weeks postinjury. It peaks at about 2 months and then evolves for an average of about 6 months. Then it reaches maturity and metabolic activity ceases.[124] The authors' patients

treated with either Etidronate within 3 weeks or Rofecoxib at any time were less likely to develop HO compared to those who took no prophylactic medication. The standard dose of Etidronate was 20 mg/kg per day for 2 weeks followed by 10 mg/kg per day for 10 weeks based on the original dosing scheme used by Stover et al[120] in their study on prophylaxis after SCI. Standard doses of Rofecoxib, Valdecoxib, and Celecoxib were 25 mg/20 mg/200 mg per day, respectively, for 8 to 12 weeks.

HO incidence appears to be markedly increased in OIF/OEF compared to prior military conflicts. Additionally, risk factors for HO development have been elucidated from the WRAMC population. Five of the risk factors are associated with increased structural trauma to soft tissue and bone. The sixth risk factor (brain injury) is neurogenic in nature and appears to have an additive effect on HO incidence when combined with structural trauma. Prophylactic medical treatment with Etidronate and Rofecoxib (no longer available) appears to decrease the probability of developing HO if started within 3 weeks of injury. To better determine a risk-benefit analysis, randomized controlled studies are needed to further determine the long-term effectiveness of both Etidronate and Celecoxib (the only COX-2 available) and identify complicating side effects, optimal dosage, and duration. However, if a decision is made to use any class of medication based on data from the Stover et al study and historical knowledge of HO's natural evolution, the authors recommend starting the medication as soon as is feasible, preferably within 3 weeks of injury.

In the authors' experience, most HO manifestations can be treated conservatively with treatments such as range-of-motion exercises and appropriate prosthetic prescription to include liner and socket modifications. However, the definitive treatment for mature HO that fails conservative therapy is surgical removal.

Heterotopic Ossification and Three-Dimensional Modeling

Because of the number and severity of the complications associated with HO, surgical excision of the abnormal bone may become necessary. Excision is an accepted treatment for symptomatic HO when conservative treatment measures fail.[116,125–127] Excision is frequently a difficult procedure because of the often intimate relationship of ectopic bone with native muscles, blood vessels, and nerves (Figure 10-2), and complications resulting from excision are common.[128] Excision of HO requires careful planning to ensure that all ectopic bone is identified and excised, to minimize the resection of muscle and soft tissue surrounding the ectopic bone, and to prevent injuries to nearby nerves and blood vessels.

Currently accepted imaging techniques, such as CT and magnetic resonance imaging, do not adequately provide a useful representation of the ectopic bone for planning and performing HO excision and for designing and fabricating prosthetic sockets. The emergence of technology that allows for the construction of three-dimensional models to display a patient's anatomy based on CT scans can now be used to plan for HO excisions and socket design.

The process that makes the construction of these models possible combines high-resolution CT, software rendering technology, and three-dimensional modeling. When construction of a model is indicated to facilitate prosthetic socket construction or surgical excision of HO, a CT scan of the residual limb is obtained using 1.5-mm slices throughout the area to be modeled. The digital data from CT images are imported to software that allows for the selection of tissues to be modeled based on pixel density (Hounsfield values). The resulting images are delivered to the 3D Systems Inc. SLA-7000, which constructs a three-dimensional

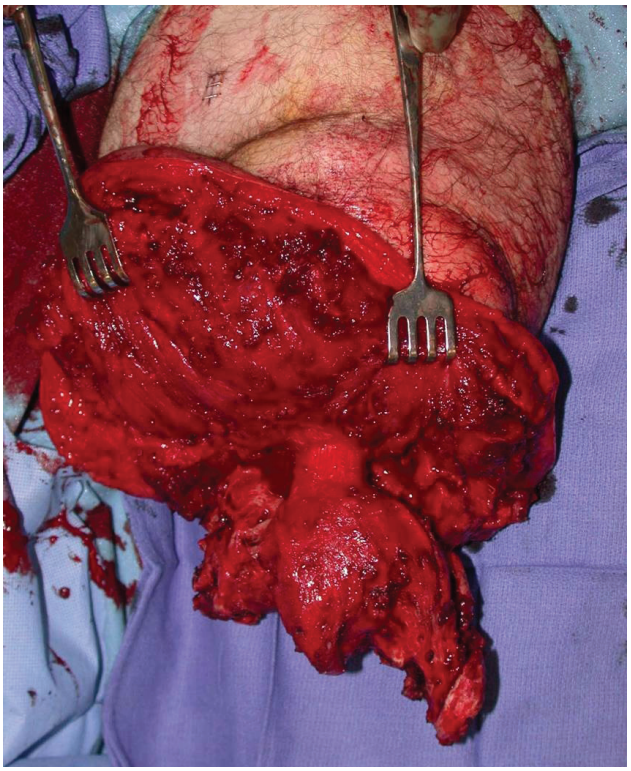

Figure 10-2. Intraoperative view of heterotopic ossification excision.

resin model of the patient's anatomy (Figure 10-3).

Several benefits and advantages result from using CT-based three-dimensional models for prosthetic socket design and surgical HO excision planning. When used for prosthetic socket design, the models improve the anatomical contouring of the socket and assist in identifying anatomic anomalies for avoidance of stress to those areas.[129] When used for planning surgical HO excision, the models helped allow for limited surgical incisions by preventing the need for complete takedown and revision of the amputation. In addition, they permitted preoperative planning of skin incisions and soft tissue revision, thereby allowing for complete HO excision while preserving enough soft tissue to adequately close the wound. The models provided a three-dimensional understanding of the ectopic bone's anatomy and, therefore, the relationship of the HO to the patient's native anatomy, which helped prevent damage to nearby nerves and blood vessels. Patients can use these models to localize pain areas in the residual limb that is attributed to specific spicules of the ectopic bone. The models also allowed for three-dimensional documentation of the extent of the HO to permit excision of all troublesome ectopic bone.[130]

In addition to being a tool for planning surgical HO excision, CT-based three-dimensional models have other uses in managing amputees and the combat wounded. Amputees returning from combat in Iraq and Afghanistan often have other traumatic injuries, many of which can hinder their progress more than the amputation. Comminuted fractures of the long bones of the extremities and pelvic fractures are common comorbid injuries. Because of the complexity of pelvic and acetabular fractures, the anatomical details and full extent of the damage are not easily demonstrated by routine radiographs. It is vital to assess the integrity of the anterior and posterior columns, hip joint spaces for debris, and the medial walls of the acetabula.[33] This assessment can often be achieved with routine CT (Figure 10-4). However, CT in conjunction with three-dimensional imaging can provide information regarding the extent of the fractures, help determine the spatial arrangement of fracture fragments, and assist the radiologist and physician understand complex fracture patterns (Figure 10-5).[131,132]

Damage to the bony structure of the pelvis often can be extensive as a result of gunshot wounds or shrapnel, forcing the patient to remain on bed rest until the fracture heals. Management consists mainly of reestablishing a joint congruence to allow for adequate weight bearing and to prevent early coxarthrosis.[133] CT-based three-dimensional models can greatly assist with assessing fracture healing because they can help monitor bony deficits in the pelvic ring until adequate continuity is established. These models, which provide accurate information on callus formation and potential areas of poor healing, can also help the patient to visualize the nature and extent of his or her injuries (Figure 10-6).

Although patients with extensive pelvic fractures remain on bed rest, it is essential for them to receive

Figure 10-3. Three-dimensional resin model of heterotopic ossification in a combat amputee.

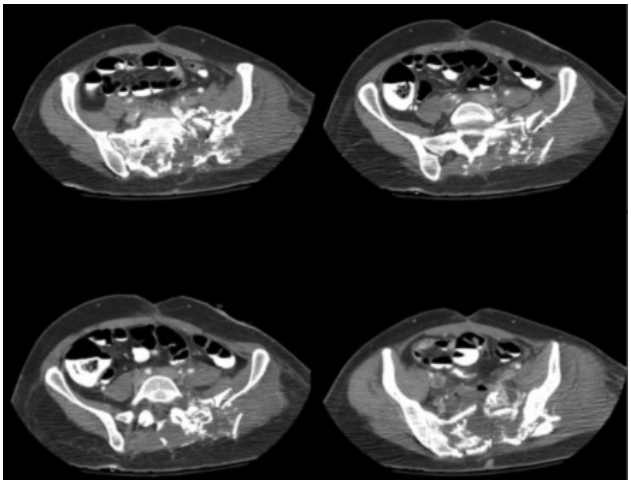

Figure 10-4. Computed tomography axial images of comminuted L5 and sacrum fractures 2 weeks postinjury.

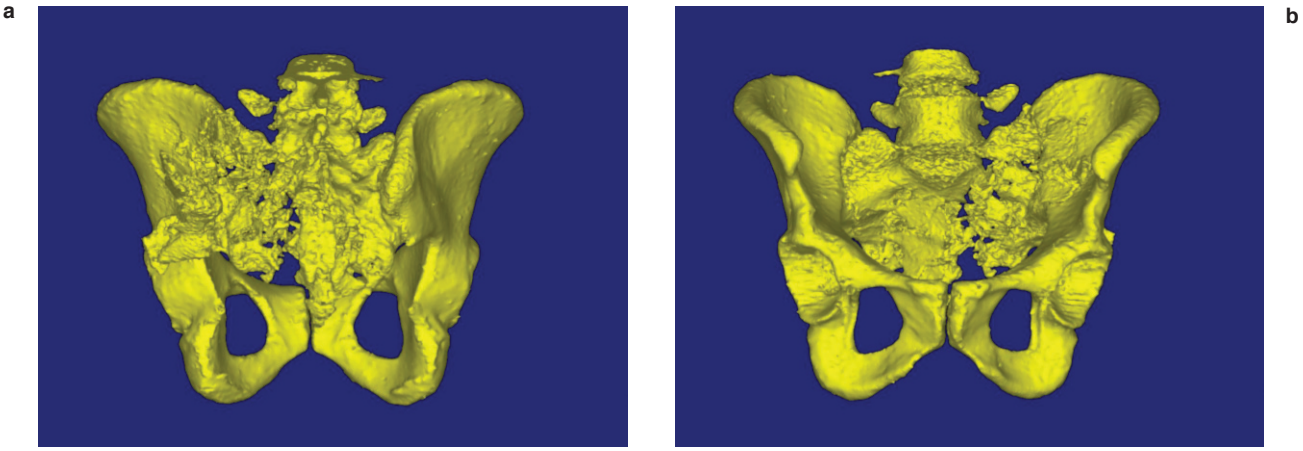

Figure 10-5. Graphic representation of three-dimensional model of the pelvis 2 weeks postinjury. (**a**) anterior view (**b**) posterior view.

bedside physical and occupational therapy to maintain upper extremity strength, lower extremity range of motion, and bed mobility. In addition, they should receive proper bowel and bladder management and their medical needs should be closely managed. Once callus formation is sufficient as indicated on CT imaging and three-dimensional models, the patient can advance to weight bearing. Training is initiated using a tilt table for improved orthostasis and the patient can ultimately progress to full weight bearing and ambulation.[134] In lower extremity amputees, fitting and casting for an initial prosthetic limb can begin while they are on bed rest. They can begin bearing weight on the prosthetic limb once improved orthostasis is achieved and they can bear weight on the intact or residual limbs.

ELECTRODIAGNOSTIC EVALUATION OF PERIPHERAL NERVE INJURIES IN COMBAT AMPUTEES/EXTREMITY TRAUMA

Patient Identification

Peripheral nerve injuries are not always apparent at the time of injury. The primary and secondary surveys are focused on life and limb preservation. Severely injured patients will be obtunded on arrival and may remain so for days to weeks. Some neurologic deficits are subtle and the diagnosis is not entertained until the patient fails to meet therapy goals or has unexplained limb pain.

All patients should have a complete neurologic exam at regular intervals for several reasons:

- It increases the likelihood that the nerve injuries will be diagnosed, especially the more subtle injuries, in the individuals who are regaining consciousness.
- It provides several data points to track the patient's recovery or failure to recover.
- These data points provide temporal context in the patient with a prolonged hospital course exposed to numerous complications.

Patients with peripheral nerve injuries can present with symptoms of pain, numbness, paresthesias, or weakness in a region or extremity. Any losses of muscle strength, sensation, or reflexes are signs of nerve injury. Swelling, increased warmth, deepened color, or lack of sweating in the distal extremity may indicate autonomic signs of nerve injury. These findings do not necessarily localize the injury to the peripheral nervous system. Central nervous system injuries can mimic or coexist with peripheral nervous system injuries.

Clinical Evaluation

The goals of the clinical evaluation are to (*a*) define the distribution of nerve(s) injured, (*b*) determine the severity of injury, and (*c*) localize the presumed site of injury. Nerve injuries can cause deficits in the distribution of nerve roots, multiple peripheral nerves, or individual peripheral nerves. In brachial plexus lesions, trunk injuries will appear as deficits in multiple dermatomes and myotomes, whereas cord injuries present as multiple peripheral nerve injuries.

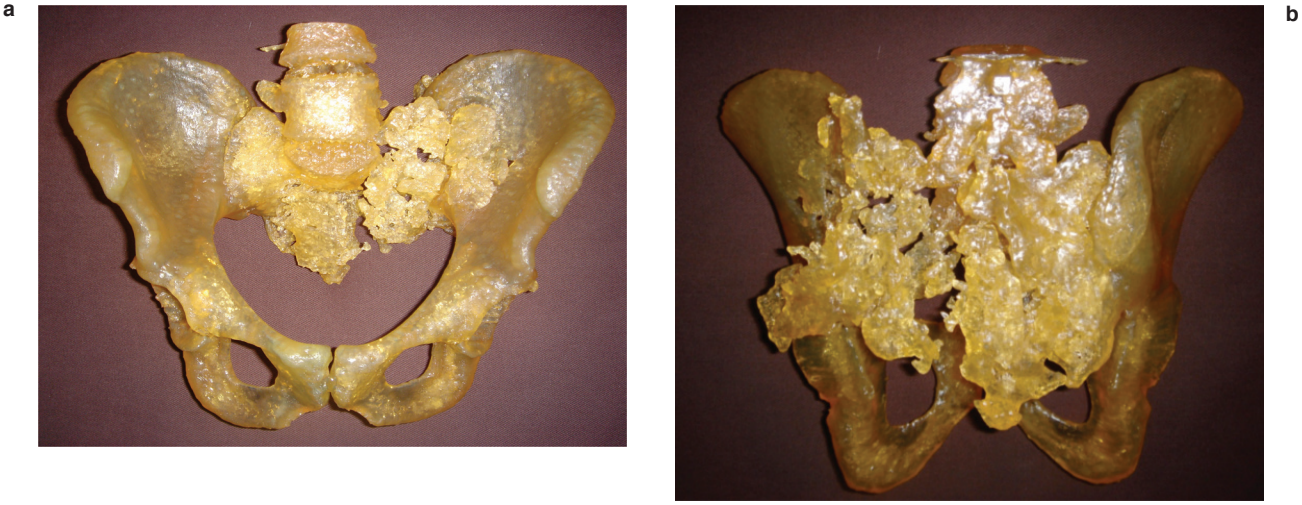

Figure 10-6. Three-dimensional model of the pelvis from Figure 10-5, 2 weeks postinjury. (**a**) anterior view, (**b**) posterior view.

For example, an upper trunk injury will present with shoulder abduction and elbow flexion weakness, and impaired sensation in the lateral forearm and thumb. A posterior cord lesion will appear as coexistent radial and axillary nerve injuries.

Different clinical and electrophysiologic severity scales exist. The initial clinical evaluation should define complete versus incomplete motor and sensory loss in a particular nerve because operative intervention is rarely required for initially incomplete injuries. When intact motor function exists in the most distal muscles innervated by a particular nerve, the injury is considered "incomplete." Key muscles in the upper extremity include the flexor digitis indicis, abductor pollicis brevis, and extensor indicis proprius for the ulnar, median, and radial nerves, respectively. In the lower extremity, the extensor hallucis longus is easily demonstrated with great toe extension for deep peroneal nerve function and palpating the adductor hallucis during great toe abduction or flexion demonstrates tibial nerve function. It is helpful to palpate the muscle being tested because substitution can sometimes create the same movement.

All patients should receive a detailed sensory exam of autonomous zones. This information can be used to support or refine the diagnosis and to help formulate an electrodiagnostic further work-up. A bedside sensory examination is very subjective and considerable anatomic variation may exist. Furthermore, after an injury adjacent nerves can expand to previously anesthetic areas. For example, if there is no motor function in median-innervated muscles but sensation is present in the palmar thumb, the injury should not be immediately categorized as incomplete.

Inspection of the trunk and extremities can provide a presumed injury site. All entry and exit wounds and surgical scars should be documented. Sometimes extensive soft tissue damage and scars exist in the distal extremity with only a single entry wound more proximal. Both must be entertained as potential injury sites. Fasciotomy scars, which are also very common in combat casualties, are usually done at the time of injury prophylactically because of vascular disruption. If the fasciotomy was performed to decompress an acute compartment syndrome, there may have been nerve injury from the compartment syndrome. Atrophy is also important because disuse atrophy is mild and more generalized, whereas denervation atrophy is profound and focal. Documentation of limb circumferences, while not validated, is a reasonable objective measurement. In the fully recovered patient with significant axonal disruption, atrophy may persist despite symmetric clinical strength. The exact location of a Tinel's sign should be documented. Distal progression of the Tinel's sign supports spontaneous recovery before return of muscle function.

A detailed history should uncover the mechanism of injury and a timeline of when nerve deficits appeared. Sometimes patients can recall immediate loss of motor function on the battlefield. Surgical reports might comment on the continuity of nerves encountered during exploration. If the nerve is found not in continuity, the ends may have been tagged and fixed to adjacent structures for future reattachment. This level of detail is often difficult to find in the medical records during medical evacuation. Patients occasionally report to

the surgeon that the "nerve is bruised" or that it is a "neuropraxia." The conclusions drawn from these particular historical reports generally mean that nerve continuity is intact.

Electrodiagnostic Evaluation

The goals of any electrodiagnostic examination are to (*a*) determine the presence or absence of nerve injury, (*b*) rule out confounding diagnoses, (*c*) localize the lesion, (*d*) characterize the nerve lesion and determine severity, and (*e*) establish prognosis.

Goals of the Electrodiagnostic Examination

1. **Determine the presence or absence of nerve injury**. Usually, the first sentence of the conclusion of an electrodiagnostic consultation is whether the study is normal or abnormal. Many individual abnormalities exist in the exam components: abnormal spontaneous potentials, abnormal motor unit morphology or recruitment, low amplitude compound muscle action potentials or sensory nerve action potentials, and conduction slowing. There are two major themes when determining an abnormal examination: (1) having multiple internally consistent abnormalities and (2) surrounding abnormalities with normality. These principles help prevent both false positive and false negative studies. False positive studies arise when conclusions are drawn on limited data. There are usually abnormalities of motor unit morphology or recruitment used to support a presumed diagnosis, ie, the self-fulfilling prophecy. False negatives arise when insufficient adjacent nerves and muscles are tested, eg, a diagnosed ulnar neuropathy that is really a lower trunk plexopathy.
2. **Rule out confounding diagnoses**. Similar to excluding a cervical radiculopathy in a patient with carpal tunnel syndrome, care must be taken to exclude more proximal or more systemic nerve lesions in patients with peripheral nerve trauma. The concept of a "double crush" nerve injury is important here. The assumption is that a nerve injury in one location has a causal relationship with a nerve injury elsewhere along a common pathway, perhaps resulting from impaired axoplasmic flow. Despite this, it is important to exclude entrapment neuropathies along an injured peripheral nerve. These represent easily treatable conditions that would otherwise interfere with recovery.
3. **Localize the lesion**. There are two ways to localize an injury on the electrodiagnostic examination. The first is to demonstrate conduction slowing or conduction block across a lesion. The second is the evaluation of the distribution of needle electromyography abnormalities. Using the second technique, there is always the possibility that "selective fasicular vulnerability" of a more proximal lesion explains the distribution of findings, eg, a sciatic injury involving only the fibers destined for the deep peroneal nerve. The electrodiagnostic localization also should be correlated with the mechanisms of injury. Both open penetrating wounds and closed blunt force injuries should be considered. This presumed site of injury is important in determining the progress.
4. **Characterize the lesion and determine severity**. The first characterization is whether the nerve injury is complete or incomplete. "Complete" does not imply nerve transection; it simply connotes that all axons are involved. However, demonstrating intact voluntary motor units in the most distal muscles of the injured nerve confirms incompleteness and at least partial nerve continuity. It is mandatory that those motor units have a rise time of less than 500 microseconds to ensure one is not looking at volume conducted motor units from nearby intact muscles. When the needle electrode exam shows positive sharp waves and fibrillations, with no voluntary recruitment of motor units, one is tempted to assume a complete injury. Performing motor and sensory nerve conductions on that nerve, distal to the presumed site of injury, allows one to demonstrate conduction block if present. A recordable response will appear if the conduction-blocked nerve is stimulated below the lesion. The partial axonal disruption explains the abnormal spontaneous potentials, and the conduction block of the remaining axons explains the inability to voluntarily recruit any motor units. The net effect is a muscle that will not activate. This demonstration of conduction block is important because it improves the patient's prognosis. The conduction block should resolve fully within 3 months.

   If the lesion is incomplete, an attempt should be made to approximate the degree of axon loss with primarily motor amplitude measurement.

Preinjury motor amplitudes would be most reliable, but are rarely available. Total body electrodiagnostic exams are not yet part of the predeployment examinations. Comparisons can be made to the contralateral limb. Although an up to 50% side-to-side motor amplitude variation exists in nonamputees, they should be considered equivalent in a patient with clear nerve injury for estimation of axon loss. This technique will underestimate the degree of axon loss after 2 to 3 months because of collateral sprouting. Unfortunately, most combat casualties do not have a true "sound side" for comparison. The contralateral limb is frequently injured or frankly absent. In those cases, amplitude comparisons with normal values with standard deviations provide a rough estimate. The utility of percentage amplitude preservation in prognosticating eventual outcome is unclear. One assumes the lower the percentage the worse the prognosis, but the real question is at what percentage is treatment altered? The answer to this typically lies with the peripheral nerve surgeon's threshold for nerve exploration. At one of the authors' institution, most incomplete injuries, regardless of percentage axon disruption, are treated conservatively.

Another characterization is the presence of ongoing reinnervation. This can be a powerful conclusion to report to the referring physician. Documenting "reinnervation" implies an improved prognosis, even if not necessarily proven. "Reinnervation" is usually documented based on the presence of polyphasic motor unit potentials. Polyphasia, however, is a normal finding in all muscles, up to a certain percentage. Quantitative techniques may add objectivity and likely improve specificity. Polyphasic motor unit potentials should also be assessed for stability. An immature polyphasic potential, either from a collateral sprout or a regenerating axon, will show instability on conventional needle electromyography. Triggering on the potentials and then superimposing them will demonstrate the stability. "Instability" is the manifestation of increased jitter and blocking seen on single fiber electromyography. When looking for stability, it may be helpful to use the "apparent single fiber" technique. Distant motor unit activity is excluded when using a concentric needle electrode and a low frequency filter of 500 Hertz.

5. **Establish prognosis**. No studies provide Class I evidence of electrodiagnostic findings and eventual outcomes. Generally, the purely neuropraxic lesions usually do well, whereas more severe nerve injuries rarely spontaneously recover. Electrodiagnostics cannot distinguish between a moderate and severe nerve injury. The diagnosis of a higher grade lesion can be based on one of four things:
   a. Direct visualization of a nerve transection.
   b. Direct visualization of a nerve lesion in continuity, but failure to conduct an action potential across the lesion site and entirely below the lesion site.
   c. Imaging, using either magnetic resonance neurography or ultrasound. Both are promising, but not readily available, and unvalidated.
   d. Failure to progress (most common). Identify the most proximal muscle that has no voluntary motor units. If axons regenerate 1 to 5 mm per day, then the maximum recovery time is 1 inch per month. One can then predict, in months, when the most proximal nonfunctioning muscle should begin working based on its distance from the presumed site of injury. Assume a median nerve injury in the distal brachium with no voluntary units in the pronator teres. If no voluntary motor units are seen in the pronator by 3 months (3 inches), then the injury is unlikely to recovery spontaneously. Assume a sciatic nerve injury in the proximal thigh. The peroneal division is complete and the tibial division demonstrates incompleteness in all muscles including the foot intrinsics. One would predict the short head of the biceps femoris would begin functioning by 12 months. The tibial division injury is incomplete from outset and will likely be followed clinically.

Mechanisms of Recovery

A nerve injury that is incomplete recovers by several mechanisms:

- resolution of conduction block (typically 0–3 months);
- collateral sprouting from the nerve terminals to innervate nearby muscle fibers that have lost their axons; and
- regeneration of the axons from the injury site.

The complete nerve injury can only recover by axonal regeneration. Once the target muscle is reached, then collateral sprouting also occurs. Muscles with some innervations may undergo muscle hypertrophy to increase strength. All patients also improve using adaptive techniques. This manifests as improvements on scales such as the functional independence measure.

Surgical Intervention

There are several types of surgical procedures to repair peripheral nerve injuries. An external neurolysis involves removal of necrotic and scar tissue from the outside of a neuroma. An internal neurolysis includes splitting the fascicles and resecting necrotic fascicles and those that cannot conduct an action potential. Those resected fibers can then be reapproximated or grafted. If no recordable action potential exists, then the entire neuroma can be resected and the nerve can be reapproximated or grafted. Neurotization involves taking fascicles from an intact nerve and performing an end-to-end or end-to-side anatamosis into the distal nonfunctioning nerve, eg, taking fascicles from the anterior interosseous nerve distal to the flexor pollicis longus and anastamosing it to the ulnar nerve near the wrist.

Nerve repairs can be immediate, early, delayed, or late. Immediate repair is done within the first hours to days for sharp, complete, but otherwise uncomplicated transections. The ends are mobilized and reapproximated. An early repair is performed several weeks after a complete injury to allow time for demarcation of the necrotic tissue to be removed. A graft may be required to achieve a tension-free repair. A delayed repair is performed between 3 and 6 months. These patients have complete deficits, but the initial Sunderland grade is unclear. They do not show recovery in the most proximal muscles as predicted by the 1 inch per month estimation. A late repair is a salvage procedure or performed for pain control. Tendon transfers are also a viable option for patients with forearm and lower leg injuries, and they are usually performed late.

Once a nerve repair—with or without graft—is performed, it must recover by axonal regeneration. Sufficient time must be given to reach the target muscles. In denervated muscle, the motor end plate degenerates sometime between 12 and 24 months. Using 18 months as a time frame will help dictate the latest a delayed repair can be performed.

Rehabilitation Intervention

The initial rehabilitation intervention is to ensure the appropriate diagnosis has been made. Repeat testing and second opinions are sometimes necessary. Patient and family education about the treatment plan and goals is important to express that progress is measured in weeks and months rather than days. Providing symptomatic treatment for neuropathic pain is covered elsewhere in this textbook (see Chapter 11, Pain Management Among Soldiers With Amputations). Interval examinations will help detect the development of complex regional pain syndrome as early as possible.

Emphasizing the importance of maintenance of range of motion is imperative. Nerve regrowth to a contracted hand is of little use. If patients are unable to demonstrate their home exercise program, then they require closer supervision. Physical and occupational therapy can assist with modalities before range-of-motion exercises, pain control, adaptive mobility, and activity of daily living strategies.

LONG-TERM EFFECTS OF LIMB AMPUTATION

The connection between health and disease is a dynamic process of salutogenesis and pathogenesis, with the individual's health dependent on the delicate balance of homeostasis.[135] The trauma associated with the combat amputee can be seen as a powerful disturbance of homeostasis because effects are experienced long after the initial injury. Longitudinal studies of traumatic amputees suggest that this population ages differently than age-matched uninjured individuals. These differences not only may be attributed directly to the amputation (altered anatomy and physiology), but also may be related to disturbance of homeostatic mechanisms. Throughout OIF/OEF, military amputee clinics have continued to focus on short-term and intermediate goals for its service members that focus on rapid function recovery and reducing impairment through adaptive techniques or assistive equipment. The main focus of the acute interventions is wound healing, pain control, prosthesis optimization, and return to high-level activities. The long-term goals of amputee rehabilitation are either return to duty or transition to the civilian community with reintegration. Regardless of initial disposition, the eventual separation of the service member from the military requires that special attention be given to the aging combat amputees and their associated greater vulnerability to certain medical complications.

Musculoskeletal Topics of Concern

Osteoarthritis has occurred in the unilateral lower extremity amputees with higher incidence than predicted based on age alone, with osteoarthritic changes found in both the ipsilateral and contralateral hips. This incidence is increased threefold in the individual with a transfemoral as compared to transtibial amputation.[135] The prevalence of symptomatic osteoarthritis of the knees has been found to be greater in amputees compared to age-matched, uninjured individuals. Factor analysis of the amputees suggests that biomechanical changes and body weight alone do not account for increased osteoarthritis incidence. In the unilateral lower extremity amputee, forces transmitted through the intact limb can be three to five times greater than total body weight (transfemoral greater than transtibial).[136] In an age-matched comparison of healthy athletic amputees and nonamputees, the incidence of contralateral knee osteoarthritis and pain was 65% greater in the amputee population.[137]

Back pain has also been shown to be a chronic and significant issue in amputees, much more than in the nonamputee population. It has been referred to as a secondary disability because 57% of amputees claimed it to be persistent and bothersome, with pain ratings of greater than 5 of 10 on the Visual Analogue Scale.[138] Functional limitations were found to be more significant in the lower extremity amputee with low back pain.[139] Bone density testing in amputees shows significant early and sustained loss over time in amputees. This is important because some studies indicate scores commonly in the range of osteopenia and often osteoporosis. The bone loss is throughout the whole body but much worse in the amputated limb.[140,141] A study by Leclercq et al correlated the loss of bone mass etiology of amputation (traumatic vs dysvascular), level of amputation (more severe bone loss when above-knee amputation), and prosthesis fit and use.[142]

Osteoarthritis and decreased levels of bone density in amputees are multifactorial. However, steps may be taken to reduce functional limitations, such as socket fit, prosthetic fit and suspension, and prescription of components, for the appropriate associated activity (eg, a multiaxial energy-storing foot for ambulating on uneven terrain). It is also vital to evaluate gait through both clinical observation and formal gait laboratory analysis. An improved understanding of the kinetics and kinematics will help the clinician and rehabilitation team provide an appropriate prescription for both prosthetic and assistive equipment and associated therapies. When feasible, eligible amputees should be referred for a formal gait and motion analysis.

Cardiovascular and Metabolic Topics of Concern

The aging amputee population has significantly worse cardiovascular and metabolic issues that appear to be directly related to their traumatic amputation and not accounted for by obesity, sedentary lifestyle, or tobacco use.[142–144] Reports demonstrate a positive correlation between a rise in norepinephrine and mean arterial blood pressure after walking in a prosthesis, a phenomenon attributed to mechanical irritation of the residual limb.[145] Studies of traumatic amputees compared to a cohort sample of the general population identify increased hypertension, ischemic heart disease, and diabetes mellitus. The traumatic amputee has a 65% greater risk of death from coronary and peripheral vascular diseases.[146,147] Rose et al hypothesized that insulin may be a causative factor in maturity-onset obesity-hypertension in his study of Vietnam War veterans who had undergone bilateral traumatic leg amputation.[148] In this study, the differences that were observed in insulin response between obese and lean bilateral above-knee amputees could not be attributed to lean body mass or physical fitness, inferring that these differences may be related to factors such as insulin-induced renal salt retention, increased sympathetic nervous stimulation, or increased cardiac inotropy.

Evidence also suggests that lower extremity amputees should be monitored for aortic aneurysms; occurring at a reported rate of 6% versus 1% in the nonamputee population. It is postulated that the asymmetric blood flow changes in the lower limb amputee lead to an unbalanced mechanical stress on the aortic wall with eventual asymmetric degeneration of the aortic wall elastic elements, resulting in an aneurysm.[149] Additionally, the metabolic costs of ambulation are substantially higher compared to the nonamputee, with much greater energy required for dysvascular amputees as compared to traumatic amputees. With aging and the aforementioned increased risk of cardiovascular disease and peripheral vascular disease in amputees, many of these demonstrate the metabolic derangements typically described in the dysvascular amputee.

The issues above underlie the importance of comprehensive nutritional, exercise, and wellness counseling for amputees. Wellness promotion and preventive measures should be part of one's lifestyle. Vigilant medical monitoring for cardiovascular diseases, including aortic aneurysms, should be routine in amputee clinics.

Endocrine Topics of Concern

The blast injuries sustained by service members in Iraq and Afghanistan are best described as polytrauma because all organ systems are affected. Comorbidities in this patient population often include TBIs, visceral organ damage, large soft tissue defects, concomitant fractures, and peripheral nerve injuries. Service members with multisystem injury are often managed acutely in the intensive care unit and require prolonged hospitalization for multiple surgical and medical issues. Previous studies in the critical care literature have elucidated the posttraumatic inflammatory response and the negative systemic effects of critical illness and polytrauma on hypothalamic-pituitary function.[150,151] Studies in patients with isolated SCI and TBI have identified associated chronic endocrinologic deficiencies, most notably hypogonadism. Total serum testosterone levels are significantly reduced in those with SCIs or TBIs.[152–155] The specific etiology of these hormonal deficiencies is multifactorial, but the question for the clinician is: once a deficiency is identified, should it be addressed through supplementation? Androgen supplementation has been beneficial in maintaining skeletal muscle following SCI[155] and has been used to augment wound healing in severe burns.[156] Deficiency of testosterone and growth hormone in the individual with TBI has been theorized to result in the observed visual-spatial impairment memory and neurovegetative symptoms such as depression. Studies evaluating the utility of hormone supplementation in TBI are pending.

The issue of sexual function and fertility in the polytrauma patient—specifically the traumatic amputee—requires evaluation. The long-term effect of endocrine derangements on reproductive health in the male and female traumatic amputee has not been described in the literature. Impaired fertility has been documented in SCI,[157] and recent animal models of SCI demonstrate that sperm integrity and genetic structure are altered following injury with an associated fertility reduction.[158] From these findings about SCIs, service members with traumatic amputations should be screened early in their periprosthetic rehabilitation to identify hormonal deficiencies and consider appropriate supplementation. In those service members considering procreation, the consultation of a fertility specialist may be appropriate in those couples having difficulty with conception.

SUMMARY

This chapter has shown that there are a number of important medical issues that must be considered in the trauma care and eventual rehabilitation of the combat amputee. Following lifesaving surgical stabilization, these issues rise in their importance and cannot be ignored. In addition to the orthopaedic and vascular surgeons, these medical issues require teamwork among a host of nonsurgical specialists from infectious diseases, physical medicine and rehabilitation, neurology, internal medicine, and hematology. In summary, whether reading for initial knowledge or review, this chapter provides an overview of basic approaches to some of the more prominent medical issues encountered in the care of the combat amputee.

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