

Chapter 36

ACUTE PAIN MANAGEMENT IN THE DEPLOYED ENVIRONMENT

CHESTER “TRIP” BUCKENMAIER III, MD*

INTRODUCTION

HISTORY OF MILITARY PAIN MANAGEMENT

PAIN “CHRONIFICATION” AND THE POLYTRAUMA TRIAD

THE ACUTE PAIN SERVICE

PAIN MANAGEMENT ON THE MODERN BATTLEFIELD

Role 1: Immediate First Aid Delivered at the Scene

Role 2: Forward Surgical Care

Role 3: Combat Support Hospitals

Roles 4 and 5: Medical Centers Outside the Theater

PAIN MEASUREMENT

CONCLUSION

**Colonel (Retired), Medical Corps, US Army; Professor of Anesthesiology, Department of Military Emergency Medicine, Uniformed Services University, Rockville, Maryland*

INTRODUCTION

“What an infinite blessing.”

—General Thomas Jonathan “Stonewall” Jackson (1824–1863)

General “Stonewall” Jackson and his Confederate army were in the process of routing the Union army during the Civil War battle of Chancellorsville, Virginia, on May 2, 1863, but he had run out of time and daylight for the attack. The general and his staff were riding in front of Confederate lines, reconnoitering the situation in hopes of pressing an evening attack to break the Union lines, when Confederate sentries mistook the scouting party for the enemy and opened fire with muskets. General Jackson was wounded in the left arm and right hand. He was removed from the battlefield by a horse-drawn field ambulance, receiving whiskey to ease the pain of his wounds. He was taken to the Confederate II Corps field hospital of Dr Hunter McGuire, where more whiskey was provided and morphine administered to further ease the general’s suffering. Early the following morning, Dr McGuire performed a left arm amputation while the general was anesthetized with chloroform. As the effects of the

anesthetic took hold, the general was reported to have murmured, “What an infinite blessing.”¹

General Jackson was most likely referring to the “blessing” of battlefield pain relief following his wounding. Contrary to popular cinematic depictions of Civil War medicine that suggested soldiers suffered surgery with little or no analgesia, morphine was in fact widely available and often used to ease the suffering of wounded soldiers. Military physicians during the war were advised to carry morphine and brandy in their pockets as their primary medications for the management of casualties.² Then as now, those responsible for providing care to Americans defending this nation have sought innovative ways to ease the suffering of battle casualties. This chapter provides the foundation for the military medical officer (MMO) to successfully implement a pain management strategy for wounded service members in the deployed environment.

HISTORY OF MILITARY PAIN MANAGEMENT

The primary active compound in opium was first isolated by the German physicist Friedrich Sertürner in 1806, and the medication was given the name “morphine” after the Greek god Morpheus. The invention of the syringe and hollow needle followed soon after in the 1850s, providing a suitable delivery system for the drug and paving the way for its use as a surgical analgesic.³ The combination of these two medical advances just prior to the American Civil War was fortuitous in light of the masses of battlefield casualties from this particularly brutal chapter in American military history. Before these advances, wounded soldiers requiring surgery had little hope of avoiding significant suffering under the knife of a surgeon. In the Revolutionary War medical text, *Diseases Incident to Armies*,⁴ John Ranby, a prominent English surgeon, is quoted:

In regard to the wounded, you should act in all respects as if you were entirely unaffected by their groans and complaints; but at the same time I would have you behave with such caution, as not to proceed rashly or cruelly, and be particularly careful to avoid unnecessary pain.⁴

In short, before the advent of the hypodermic needle and morphine, those wounded in America’s wars could hope for little more than a speedy surgeon willing to avoid unnecessary pain. Prior to the

Civil War, anesthesia and analgesia for soldiers was at best rudimentary. The lack of adequate pain control served as a significant impediment to battlefield surgical development; operations were reserved for the direst of circumstances and the surgery was often as deadly as the inciting wound. As General Jackson so eloquently noted, the ability to manage the pain of combat wounds was indeed a blessing. The miracle of analgesia with morphine and other opioid medications was certainly a significant advancement in battlefield surgical management, although this therapy would prove to have a decidedly unhealthy side. Serious consequences associated with chronic opioid use for pain were recognized following the Civil War. In their 1928 book, *The Opium Problem*, Terry and Pellens noted that “following the Civil War the increase in opiate use was so marked among ex-soldiers as to give rise to the term ‘army disease,’ and today in more than one old soldiers’ home are cases of chronic opium intoxication which date from this period.”⁵ It has been suggested that the widespread use of morphine, during and long after the Civil War, gave rise to the first large-scale drug addiction problem within the United States. Spikes in drug abuse have followed every major US conflict since.²

Interestingly, the Civil War provided some classic descriptions of chronic pain conditions, such as “phantom limb pain” and “causalgia” (termed “complex

regional pain syndrome" today). S. Weir Mitchell, a neurologist, insisted his patients had a form of physical illness, manifested by the strange pain behaviors noted above, that seemed to persist long after their wounds had healed. Unfortunately, this viewpoint changed by the 1920s with the development of "specificity theory," which postulated the experience of pain had to be associated with a specific noxious stimulus. Pain sufferers who did not meet these strict criteria were presumed to be malingerers or drug abusers.⁶ At this point, morphine was highly regulated, and chronic pain patients were often limited to psychotherapy or neurosurgical procedures (resection or ablation of nerves) with poor and often debilitating results.⁶

Although attitudes regarding the treatment of acute and chronic pain continued to evolve, morphine remained the gold standard for battlefield analgesia during World War II. Henry K. Beecher, an anesthesiologist in the US Army who served in the North African and Italian campaigns, provided the first wartime clinical investigations specifically on the issue of pain from battlefield wounds.⁷ Dr Beecher made several salient observations related to morphine use at the point of battlefield injury, during initial casualty care, and its impact on casualty outcomes. First, Beecher noted that at the point of injury, medics routinely administered morphine prophylactically, versus the administration after an assessment of a casualty's actual complaint of pain. Beecher noted that this approach might adversely impact casualties as their treatment continued, particularly those who were hypovolemic. He observed that intramuscular injection of morphine in patients with low blood pressure from wounding often failed to decrease pain, prompting additional dosages. When the patient was eventually warmed and normal circulation reestablished at the field hospital, the unabsorbed deposits of morphine in the muscle entered the circulation, resulting in morphine toxicity. Furthermore, while advocating for the more responsible use of morphine on the battlefield, Beecher developed the first concept of multimodal pain management in battlefield casualties by recognizing the importance of regional nerve blocks, proper splinting and bandaging, and emotional care as all being important components of pain management in the wounded.

As World War II ended, a young anesthesiologist named John Bonica was struggling to run an anesthesia service at the newly built Madigan Army Hospital in Washington State. Bonica observed a growing number of returning soldiers with healed wounds but baffling "lesionless" chronic pain problems. He was astonished at the general lack of information on the management of these pain conditions either in the literature or from experienced colleagues in other medical specialties. Dr

Bonica took it upon himself to read anything he could find on chronic pain and instituted regular meetings with colleagues to discuss the management of pain patients.⁸ This postwar experience thoroughly convinced Dr Bonica that complex pain problems required a coordinated, multidisciplinary approach, which later led to his establishment of the first pain clinic at the University of Washington, in 1961.⁹ Dr Bonica is further credited with the first comprehensive textbook on pain management, *The Management of Pain*,¹⁰ now in its fourth edition. It would not be an overstatement to suggest that the modern practice of pain medicine was forged in the minds and experience of those caring for American war wounded.

Although innovation in battlefield surgery and anesthesia progressed rapidly following World War II, scant attention was afforded casualties with pain on American battlefields beyond the provision of morphine. Prevailing attitudes considered acute pain a natural symptom of wounding that would be alleviated through appropriate management, healing, and rehabilitation. Perhaps this explains why the evolution of pain management on the American battlefield stalled with morphine, a solution from the Civil War. The recognition that acute pain influences the development of chronic pain is a relatively recent concept, and the mechanisms involved in the transition of acute to chronic pain, or "chronification" of pain (see below), remain poorly elucidated.¹¹

At the onset of the conflicts in Afghanistan and Iraq following September 11, 2001, the American military deployed into a 21st century combat casualty care environment almost exclusively with morphine, a 19th century pain management solution. Although morphine maintained its historical reputation for treating combat trauma pain, it proved to be a poor fit given the recent evolution of modern patient evacuation capabilities and treatment doctrine. Previously, common practice had been to hold the wounded for days in theater until they were clinically stable for transport. Patients today are now being held only long enough to be stabilized for transport to the next node, or role, of higher medical treatment capability. During the Vietnam War, the average time from point of injury back to the United States was 45 days, whereas today the average time is only 4 days.¹² The rapid transition of casualties by evacuation aircraft to higher levels of medical capability has been considered a key factor in the historically low died-of-wounds rate, less than 10%, established in Iraq and Afghanistan.¹²

While the improved aeromedical evacuation chain has been a remarkable success, it resulted in unexpected consequences in terms of pain management. Military aircraft used for casualty transport present dif-



Figure 36-1. Inside a C-17 Air Force medical evacuation flight from Afghanistan.

difficult environments for administering pain care. Pain experienced from combat wounds tended to be exacerbated in the loud, vibrating, cramped, and bouncing interior of an aircraft in flight for extended distances (Figure 36-1). Aeromedical personnel, constrained early in the war to morphine for pain management, were significantly challenged by limitations in monitoring capability, space, and equipment. Managing respiratory complications associated with morphine in this environment can be life threatening; therefore, many patients arrived at their destination with inadequate pain control.¹³ In 2003, the US Army surgeon general, Lieutenant General James Peake, called for innovative pain solutions to address a number of wounded soldiers reportedly arriving in Landstuhl, Germany, from Iraq and Afghanistan in “agony.” Peake’s directive resulted in the first deployment of medical personnel and equipment with the express mission of improving evacuation pain management.¹⁴

For some time prior to September 11, 2001, military anesthesia leaders had been considering an expanded role for regional anesthesia (RA) and local anesthetics on the modern battlefield. Although its utilization in civilian medicine was limited to several academic medical centers, recent RA advances with new needle and peripheral nerve catheter technology, peripheral nerve stimulation, and microprocessor-driven infusion pumps had enhanced the value of RA as a viable battlefield anesthetic and analgesic. Furthermore, the military’s use of RA was expanding for routine surgery in the United States, while military medical missions to underserved regions of the world were recognizing other benefits of RA. Specifically noted were improved patient hemodynamic stability, safety, small logistic and equipment support requirements, and profound perioperative analgesia, especially when continuous peripheral nerve block (CPNB) catheters were utilized.¹⁵

Based on the military’s initial experience with RA and a review of casualty data, initial efforts to improve casualty evacuation pain management were centered on bringing advanced RA to the modern battlefield. In a query of wound types in 3,102 casualties from October 2001 to January 2005, 54% were orthopedic extremity wounds recognized as particularly suited for RA and CPNB management.¹⁶

In 2003, the first CPNB was placed in an American casualty who had sustained extensive injury to his left calf from a rocket-propelled grenade (Figure 36-2). Despite intravenous administration of morphine sulfate, 18 mg titrated over 60 minutes, the patient complained of the highest level of pain on a verbal analog scale (10 out of 10) upon arrival at the 21st Combat Support Hospital (CSH) in Balad, Iraq. As part of his operating room anesthetic management, continuous left lumbar plexus and continuous sciatic nerve catheters were placed, reducing his pain to zero, and debridement of the wound was performed under light sedation with the patient spontaneously ventilating. Following this first operation, the patient traveled to Walter Reed Army Medical Center in Washington, DC, via Landstuhl Regional Medical Center (LRMC), Germany, with the majority of his analgesic needs handled through continuous infusions of 0.2% ropivacaine through the CPNB catheters. The CPNB catheters placed in the Iraq CSH were maintained for 16 days and used to establish surgical level blocks for four additional operations.¹⁴ This first experience led, within a few years, to routine use of RA and CPNB in Iraq and Afghanistan in hundreds of casualties. Although a complete description of RA and CPNB use on the battlefield is beyond the scope of this chapter, an excellent resource for understanding RA on the modern battlefield can be found in the *Military*



Figure 36-2. Typical wound managed with continuous peripheral nerve blocks at a combat support hospital.

Advanced Regional Anesthesia and Analgesia handbook, the first military medical text devoted to the acute pain management of battlefield casualties.¹⁷

RA, while transformational for the pain management of extremity wounds, is not appropriate for many other injuries that were left with morphine as the sole analgesic option. However, in the process of fielding RA in the evacuation system, the door was opened for an expanded evaluation of acute pain management across all roles of care. Medical officers from all three

uniformed services, spurred by the need to improve pain care for the wounded, ill, and injured, began to work through their inter-service differences to develop a synchronized strategy to address pain management. This was fortunate because the general lack of historical attention to casualty pain management and the overreliance on morphine monotherapy for pain on the battlefield was contributing to later recuperation problems for service members and veterans at home as they continued their rehabilitation and recovery.¹⁸

PAIN “CHRONIFICATION” AND THE POLYTRAUMA TRIAD

Although relief of pain and suffering following wounding has always been considered a noble act and ethically sound medical practice, pain has historically been understood to be an acute symptom of wounding or disease that would resolve as the casualty recovered and rehabilitated. Woolf¹⁹ proposed that pain be divided into two broad categories: adaptive and maladaptive. Adaptive pain is protective against injury, promotes survival when injury has occurred, and is self-limiting. Maladaptive pain, on the other hand, is a pathologic response by the nervous system to noxious stimuli and is a manifestation of pain as a disease. Only in the past few decades have physicians begun to understand that poorly managed acute pain (adaptive) can have a negative impact on recovery and lead to debilitating chronic pain (maladaptive). Evidence is mounting that endogenous and exogenous factors can influence pain signal descending pathway modulation within the spinal cord and possibly influence “chronification” of acute pain into chronic pain.²⁰ Individuals who exhibit symptoms consistent with pain chronification develop common brain changes in areas known to manage nociceptive input or pain regulation. It has been suggested that these brain changes represent a pain chronification signature that should be reversible with adequate pain management.²¹ However, the myriad influences impacting the chronification of pain remain incompletely and poorly understood. Rollin Gallagher, MD, editor of *Pain Medicine*, has modeled the chronification of pain as a cycle that begins with acute injury and cascades into a series of pathological central nervous system aberrant changes. These

changes can be mutually reinforcing in a vicious circle and lead to the disease process of chronic pain with its attendant physical, psychological, and social disability (Figure 36-3).

The impact of pain chronification on a wounded service member’s recovery and rehabilitation is often devastating. Moreover, unlike the obvious disability associated with amputation, broken bones, and wounds that engender public sympathy, the burden of chronic pain is often invisible to the public; those carrying this burden often do so alone with little public or professional empathy. Development of chronic pain can further exacerbate other common wartime injuries such as posttraumatic stress disorder (PTSD) and traumatic brain injury (TBI), which are often described as signature injuries from the recent conflicts. Lew et al²² recently examined the medical records of 340 consecutive veterans being treated for polytrauma to determine the incidence of chronic pain, PTSD, and TBI in this population. They noted that 81.5% of this population complained of chronic pain (compared to 68.2% with PTSD and 66.8% with TBI). Furthermore, 41.2% of the cohort had all three conditions simultaneously. This group suggested that the association of chronic pain, PTSD, and TBI represents a polytrauma clinical triad, and most patients diagnosed with one condition will have the others in combination. However, although considerable attention and investment has been directed towards PTSD and TBI research and treatment, comparatively little investment has been afforded chronic pain in the same period, even though it is the more common complaint among trauma victims.

THE ACUTE PAIN SERVICE

The fact that opioids have historically served (and continue to serve) in the modern era as a cornerstone of pain management following combat wounds is understandable, because this class of medications has few peers in terms of the speed and intensity of the analgesia produced. As noted earlier, the use of this

medication has had a long association with military medicine, and more severely wounded veterans are surviving than at any time in history. Unfortunately, the consequences of opioid monotherapy for pain management is becoming a problem as significant, and in many cases worse, than the pain condition being

Chronification: The Chronic Pain Cycle

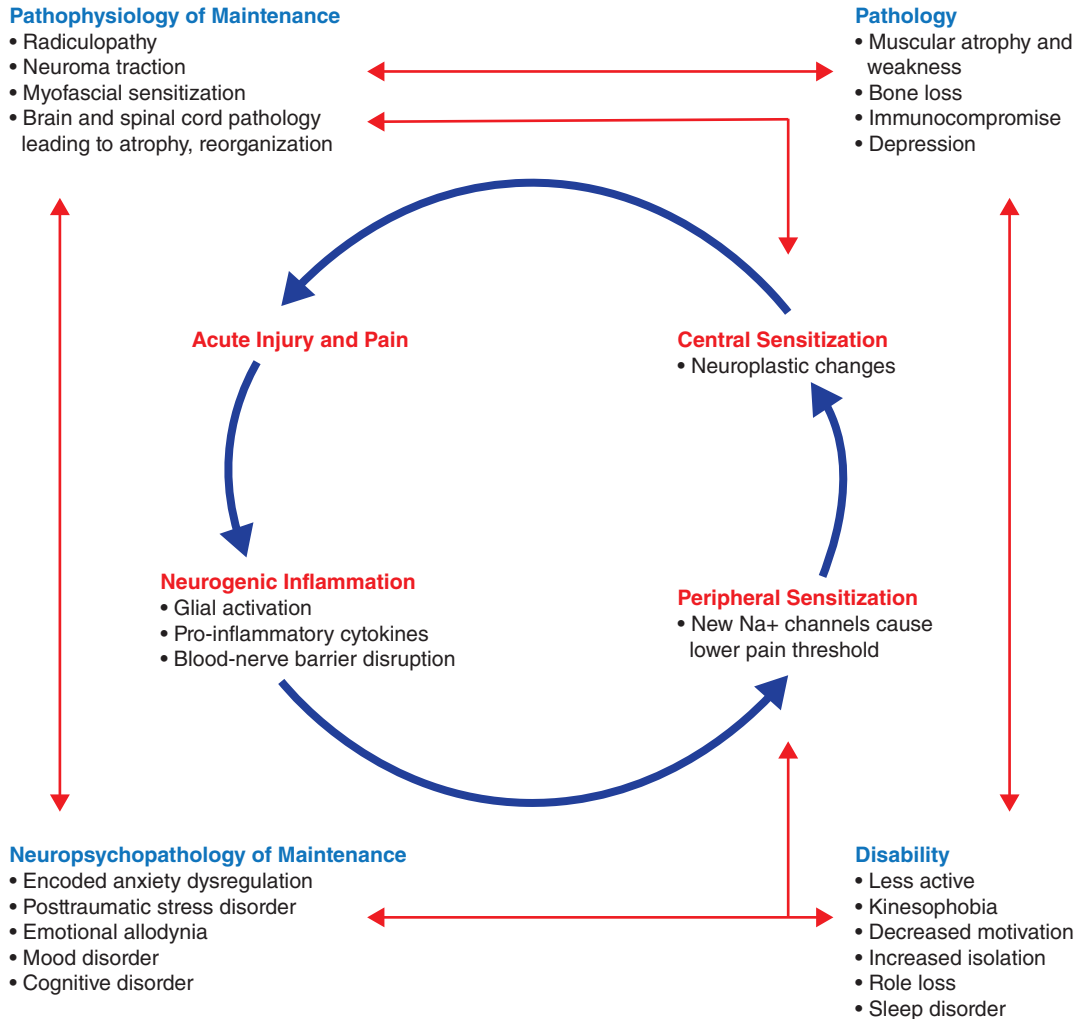


Figure 36-3. “Chronification”: the chronic pain cycle. Reproduced with permission from: Gallagher RM. Pharmacologic approaches to pain management. In: Ebert M, Kerns R, eds. *Behavioral and Psychopharmacologic Pain Management*. New York, NY: Cambridge University Press; 2011:139.

treated. Beyond the usual acute side effects of nausea, constipation, dependence, and potentially deadly respiratory depression, the use of opioids for protracted periods can lead to a host of other issues. Chronic opioid use has been associated with reductions in sex hormones in men, termed opioid-induced androgen deficiency (OPIAD), that can result in significantly higher levels of depression, fatigue, and sexual dysfunction.²³ Other conditions associated with long-term opioid use include osteoporosis, immune function suppression, and cognitive impairment.²⁴

Obviously these conditions significantly detract from the recovery and rehabilitation of a casualty from combat trauma. Even more disconcerting is the

mounting evidence that ongoing use of opioids for pain may paradoxically decrease the threshold for a patient’s tolerance of noxious stimuli. Although the exact mechanism for this phenomenon is incompletely understood, it is likely a combination of both peripheral and central nervous system changes influenced by chronic opioid therapy.^{24,25} Mirroring the national opioid misuse and abuse trends, the military has experienced an increase in opioid-related problems that have likely been magnified by the stress associated with the last 18 years of conflict.²⁶ The medical community’s continued overreliance on opioids as a single approach for managing pain has created an epidemic of prescription medication abuse and diversion within

the United States. In 2009, the rate of deaths due to unintentional drug overdoses surpassed those caused by motor vehicle crashes.²⁷

As evidence has become increasingly unfavorable toward opioid monotherapy on the battlefield, coupled with recent successes in managing complex trauma with CPNB and local anesthetics, the need for a systematic approach to pain for casualty evacuation has become more apparent. While CPNB catheters have clearly demonstrated efficacy in the management of polytrauma pain without the significant side effects associated with opioids, RA techniques and other advanced pain management options require trained medical personnel and logistics support at all roles of care in the evacuation chain.²⁸ Fortunately, as chronification of acute pain increasingly became considered as a disease process, efforts in both military and civilian medicine began establishing acute pain management infrastructure through establishment of an acute pain service (APS).

The APS provides the training, medical logistics, and organizational framework for physicians, nurses, and other support personnel to diagnose and treat acute pain as a pathophysiologic ailment.²⁹ Most importantly, the APS infrastructure facilitates the use of multimodal analgesia for patients based on their individual problems, within the context of increasingly complex pain issues associated with trauma and the modern perioperative environment. Multimodal analgesia is defined as the use of two or more medications or techniques that produce analgesia by different mechanisms. The advantage of this approach is that the overall analgesia is superior to what would have been achieved using any single drug or procedure (monotherapy), while the unwanted side effects of any one treatment element are minimized because of reduced reliance, and thus a smaller dose, of any one element.^{30,31}

Concurrent with the improvements in managing acute pain through APS establishment in major US hospitals has been the realization that aggressive and effective acute pain management reduces postoperative morbidity.³² Furthermore, effective control of acute pain reduces the cascade of unwanted physiologic consequences (see Figure 36-3) associated with unmanaged nociception, which adversely impact recovery and rehabilitation and can induce chronic pain.^{33,34} Persistent postsurgical pain, defined as pain lasting 3 to 6 months after surgery, is present in 10% to 50% of surgical patients, and can lead to debilitating chronic pain in 2% to 10% of these patients.³⁵

Despite this alarmingly high incidence, little is generally known or accepted on who is at risk for developing chronic pain following trauma or surgery, or how to effectively manage acute pain to avoid chronification. It is understood that acute pain chronification is a complex problem involving many patient factors in the perioperative and recovery periods that contribute to persistent postsurgical pain and, in some patients, chronic pain.³⁶ Certainly a patient's genotype is an important determinant of susceptibility to chronic pain development, but epigenetic modifications of gene expression that are influenced by exposure to toxins, medications, diet, and other physiologic and psychological stressors can also impact a patient's unique predisposition to developing chronic pain after trauma or surgery.³⁷ This emerging understanding of the complexity and importance of effective pain management in a patient's overall healing, along with the requirement to address the needs of the wounded, ill, and injured from the Afghanistan and Iraq wars, has led to a reemphasis on the management of pain in war casualties on 21st century battlefields.

PAIN MANAGEMENT ON THE MODERN BATTLEFIELD

In 2009, following increasing reports of prescription medication abuse and diversion among the Army wounded assigned to the Warrior Transition Units, as well as continued concerns with the lack of a clear pain management strategy, the Army surgeon general, Lieutenant General Eric Schoomaker, chartered the Tri-Service Pain Management Task Force (PMTF). Its mission was to review military pain management capabilities and practices and develop recommendations for a comprehensive pain management strategy. The resulting PMTF report (2010) outlined over 100 recommendations for a pain management strategy that is "holistic, multidisciplinary, and multimodal in its approach, utilizes state of the art/science modalities

and technologies, and provides optimal quality of life for soldiers and other patients with acute and chronic pain."³⁸ This effort has further increased the military health system's reemphasis on pain management, both acute and chronic, throughout the casualty evacuation chain and within military treatment facilities.

Casualty care on the modern battlefield is organized into four roles of care (previously known as levels) that denote increasing medical capability from point of injury back to the United States (see Chapter 14, Introduction to Health Service Support).³⁹ A discussion of improvements in pain management of casualties from recent conflicts is best described within this framework of the roles of care.

Role 1: Immediate First Aid Delivered at the Scene

Role 1 care is at point of injury and focused on self-aid and buddy aid. One of the most basic and important actions the individual soldier can undertake to reduce the impact of pain and enhance resilience following wounding is through efforts directed at achieving better personal health and fitness prior to deployment (see Chapter 19, The Evolution of Human Performance Optimization and Total Force Fitness). This concept is embodied by the Army Medical Command's Performance Triad campaign, which is designed to establish healthy lifestyle habits with focus on physical activity, appropriate nutrition, and adequate sleep.⁴⁰ Essentially, a healthy person will be better prepared to tolerate the physical and psychological stress associated with acute pain, and thus better able to resist pain chronification.

While morphine continues as the primary, gold standard analgesic for combat medics, there have been significant changes to the Role 1 approach to analgesia. One example is the inclusion of a chapter on pain assessment and control (Chapter 30, Basic Medical Skills) in the *Special Operations Forces Medical Handbook*, 2nd edition, which serves as a primary medical information source for combat medics.⁴¹ This resource provides information on the analgesics taken by medics into battle, along with the "dos" and "don'ts" of analgesic management in this complex and dangerous environment. The primary annual skills sustainment courses for medics and corpsmen still have a heavy focus on morphine as the primary analgesic. However, Tactical Combat Casualty Care (TCCC) guidelines, endorsed by the Department of Defense, offer a much broader range of analgesic options.

A number of recent developments have occurred in acute pain management of combat casualties far forward on the modern battlefield. One of the more novel approaches, developed by US Special Forces, involved issuing individual first aid kits with combat pill packs to be used in the event of wounding in the combat environment. Essentially, soldiers were instructed to self-administer the medications as soon as practical if painfully wounded and alert enough to open the pack, while remaining in the fight. The packs contained a cyclooxygenase-2-selective nonsteroidal antiinflammatory drug (NSAID), meloxicam 15 mg, and acetaminophen 650 mg, in addition to the antibiotic gatifloxacin.⁴² Neither of the pain medications impact platelet function when given as single doses, and therefore do not impede clot formation following wounding.^{43,44} With brilliant simplicity, this approach granted the casualty instant access to pain management at the point of injury without reliance on another,

likely otherwise occupied, soldier. Additionally, these medications have no clinically relevant impact on cognition, allowing the wounded soldier to "stay in the fight" while still establishing a non-opioid analgesic foundation that can be built upon through the roles of care when the casualty is evacuated. While the pill packs are not currently carried by all soldiers, many combat medics and corpsmen have these medications available to treat battlefield casualties at the point of injury.

For casualties in pain who are unable to fight and do not require intravenous access, oral transmucosal fentanyl citrate (OTFC), 800 µg transbuccal (a "fentanyl lollipop"), is frequently used by combat medics in the field.⁴² Kotwal et al⁴⁵ studied 22 hemodynamically stable casualties with uncomplicated orthopedic trauma and concluded that OTFC was an effective, rapid-acting analgesic alternative for trauma in the combat or austere environment. The ability to administer the medication via the oral mucosa, negating the need for vascular access, is a definitive advantage. One patient in this series did experience hypoventilation, which remains the primary issue of concern for all opioid medications in this environment. Therefore, medics continue to be advised to monitor patients closely following any opioid administration while keeping naloxone readily accessible.⁴⁶ The most common side effect associated with this approach, as with other opioid-based methods, is nausea.⁴⁷ Although OTFC has demonstrated significant efficacy in managing acute trauma pain, like morphine, the risks associated with opioid medications are not resolved with this delivery method.

One of the most interesting developments from the recent conflicts is the use of ketamine as an analgesic alternative to morphine on the battlefield. In the same class of drugs as phencyclidine (PCP), ketamine is termed a dissociative anesthetic and has been described as producing a cataleptic state, amnesia, and intense analgesia without depression of the respiratory rate or blood pressure at low doses.^{48,49} Additionally, ketamine is a noncompetitive antagonist of the *N*-methyl-D-aspartate (NMDA) receptor, which is activated by peripheral nociception, leading to hyperexcitability of dorsal root neurons, which is thought to contribute to central sensitization and the chronification of pain.^{49,50} The most common side effects associated with ketamine administration are psychedelic emergence phenomena, including feelings of floating, vivid dreams, hallucinations, and delirium.^{51,52} These issues can be minimized or eliminated if the infusion dose of ketamine utilized is low (< 2.5 µg/kg/min) and certainly these issues are not as troublesome as those associated with opioid or

NSAID use.⁵³ Eastridge et al, in a review of 4,596 Iraq and Afghanistan combat casualties from October 2001 to June 2011, identified hemorrhage as responsible for 90% of deaths from potentially survivable wounds and recommended “providing a battlefield analgesia option that does not cause respiratory depression or exacerbate hemorrhagic shock.”⁵⁴ Ketamine has many attributes that fulfill these conditions.

The flexibility of ketamine as the principle anesthetic in military situations was demonstrated during the Somalia civil war in 1994 and in north Uganda in 1999. The conditions in these conflicts were so austere that patient monitoring during surgery consisted of counting respirations and the heart rate while adjusting the ketamine drip rate based on established parameters every 3 to 5 minutes. This was accomplished with ancillary staff of variable anesthesia training and experience.⁵⁵ In the author’s own experience in 2009, while deployed as an anesthesiologist at Camp Bastion, Afghanistan, two options were available for providing analgesia during initial trauma assessments: morphine and ketamine. In every case where I was the lead trauma anesthesiologist, I selected ketamine over morphine to provide analgesia due to its consistent analgesic effectiveness without the hemodynamic complications of respiratory depression and hypotension associated with morphine. Ketamine was also extremely useful when a chemical restraint was indicated to prevent patients from injuring themselves, or in support of procedures or imaging studies where a comfortable and motionless patient was desirable. In the recent conflicts, ketamine has been determined to be at least as effective as morphine for providing analgesia at point of injury and during initial evacuation.⁵⁶ In a study of 48 healthy volunteers who were asked to perform common military tasks after exposure to morphine 10 mg versus ketamine 25 mg given intramuscularly in the deltoid muscle, ketamine was associated with more reports of side effects (dizziness, poor concentration, or feelings of happiness generally), although performance decrements between the two medications were minimal.⁵⁷ Intranasal delivery of ketamine has also been evaluated, removing the need for vascular access.⁵⁸

These properties of ketamine make it an ideal Role 1 analgesic, and recent changes to the TCCC guidelines for pain management now include ketamine for the first time.⁵⁹ Ketamine, either 50 mg intramuscular or intranasal, or 20 mg intravenous or intraosseous (administered slowly), is recommended as an additional option to opioid therapy for moderate to severe pain in Role 1 conditions. In a review of 228 Afghanistan casualties evacuated from the battlefield by rotary aircraft from October 2012 to September 2013, the most com-

mon analgesic used was ketamine, closely followed by morphine; when two analgesics were employed, ketamine and morphine were most often used.⁶⁰

Role 2: Forward Surgical Care

Role 2 facilities provide enhanced resuscitation services compared to Role 1, with the important addition of surgical assets to provide damage control resuscitation and surgery, as well as casualty collection and sorting efforts. These facilities are the first level of care where blood and blood products are available for trauma resuscitation.⁶¹ Analgesic options at this level are similar to Role 1, with the addition of general anesthesia and single injection RA when indicated.

An interesting development from the recent conflicts is the use of acupuncture in the management of acute pain and stress issues in the far-forward Role 1 and 2 environment. Working in the deployed military environment is stressful and hard on the body, without even considering conditions experienced in actual combat. From wearing 40 pounds of body armor and equipment, to walking or riding in difficult terrain, and being constantly on alert for danger, among many other taxing wartime events, soldiers have plenty of reasons to develop painful conditions. Military healthcare providers have found acupuncture to be a safe and useful therapy in pain and stress management for soldiers on the modern battlefield.⁶² Acupuncture requires minimal equipment to perform, is associated with minimal (mostly minor) side effects, and has no abuse potential. The increased use of acupuncture, particularly auricular acupuncture, in the care of soldiers has been a unique feature of the medical response to the wars in Iraq and Afghanistan. A battalion aid station serving 500 Seabees deployed to Iraq from September 2006 through March 2007 managed 132 individual patients with acupuncture for a variety of issues, and 80% of these patients required no additional medications such as antiinflammatories or analgesics.⁶³ These attributes have prompted some medical leaders to suggest acupuncture training and services should be a routine component of the military response to disaster or war.⁶⁴

Despite published and anecdotal reports of the successful application of acupuncture on the modern battlefield, the general consensus is that an appropriate evidence base to support standard acupuncture care protocols in the military is lacking.⁶⁵ This is not to suggest a lack of evidence to support acupuncture in the management of a variety of conditions; rather, there remains a general dearth of experience and system support within the military to develop an understanding of acupuncture’s role in military

medicine. This situation is changing as the military seeks non-opioid options for analgesic care in austere conditions. Although acupuncture has been used sporadically throughout the military since the 1980s, there has been a major educational and clinical transformation in the use of acupuncture during the past decade.⁶⁶ Initial investment into DoD-wide acupuncture training and credentialing has been through the introduction of battlefield acupuncture (BFA), an auricular acupuncture protocol for pain that is taught to all levels of provider within the military.⁶⁷ BFA is a series of five auricular points, called cingulate gyrus, thalamus, omega 2, point zero, and shen men (Figure 36-4), in which semipermanent needle studs are placed to reduce pain and stress.⁶⁸ This program was designed to socialize both patients and providers to the use of acupuncture in military care settings while adding a nonpharmaceutical complementary method for treating pain. Although considerable additional research and experience is needed before acupuncture in the military can be considered routine, it is the most developed integra-



Figure 36-4. Battlefield acupuncture auricular points. Points are usually placed in the following order: cingulate gyrus, thalamus, omega 2, point zero, and shen men (CTOPS). Photograph courtesy of Richard C. Niemtzw, MD

tive medicine approach within the federal medicine system today and will likely be a common approach to managing pain in the future.

Role 3: Combat Support Hospitals

The goal of both Role 1 and 2 care efforts is the stabilization of the casualty for evacuation to a Role 3 facility within the war theater. Role 3 facilities have the major surgical specialties represented, full anesthesia capability, intensive care, diagnostic imaging, laboratory, and blood bank services available. Role 3 represents the highest level of care within the war theater and the first opportunity for restorative care, including comprehensive pain management.

Perhaps one of the most significant concepts to develop from the recent wars is the realization that effective pain management begins at point of injury, must operate as a continuum throughout the roles of care, extends into the casualty's evacuation to the United States, continues through rehabilitation in medical centers, and stretches into the rest of their lives.⁶⁹ This is a considerable responsibility for any healthcare system, but shirking this effort can, and often does, destroy the quality and productivity of the life that was saved on the battlefield. (This is not to suggest that military healthcare providers have ignored pain and suffering in the past; in fact, pain management has been considered the general responsibility of every healthcare provider. Superficially this approach may appear to be a reasonable, but when everyone is held responsible, no one can be held accountable when pain is an issue for the wounded soldier.)

Despite contemporary understanding of the detrimental impact of inadequate pain management on rehabilitation and recovery following trauma or surgery,⁷⁰ adequate and continuous pain management remains a significant challenge for the military, particularly in the deployed or evacuation environment. Sophisticated management of pain, beyond the application of opioid monotherapy, requires establishment of an APS of dedicated physicians, nurses, and support personnel who are both responsible and accountable for casualty pain management within the CSH. Through a collaboration between US and United Kingdom military medical services, a demonstration APS was established at the Camp Bastion, Afghanistan, CSH in 2009.⁷¹ The British CSH leadership established pain management as a key indicator of care quality at the facility during the project. APS personnel consisted of a physician leader with specialty training in acute pain management and RA, as well as pain nurse champions within each care ward in the hospital. The team was augmented with specialized equipment dedicated

to pain management, including pain infusion pumps, RA catheters and equipment, peripheral nerve stimulators, and a portable ultrasound machine.

During this particular demonstration, approximately 455 trauma cases were managed by the CSH trauma team, and the APS physician rounded daily with the team as the pain consultant. Unusual or difficult acute pain cases were managed directly by the APS, although all casualties received a multimodal pain care plan. Table 36-1 outlines the frequency of intravenous and oral analgesic medications that were used in this patient cohort. Of the 71 casualties managed directly by the APS in this project, 51 (71.8%) received RA as part of their multimodal pain plan. The majority of these patients had traumatic amputations or limb injuries. The average improvement in pain scores (for those able to report), based on the casualties' recall estimate of their pain at point of injury, was 51.9% (\pm 31.2). A general survey of healthcare providers at the CSH during the project period was also performed to evaluate their perceptions of the value of the activity to overall care.⁷² The survey consisted of items designed to appraise staff impressions of APS outcomes, com-

plexity of care, decision-making support, and pain management education. Generally the survey revealed considerable enthusiasm for the establishment of the CSH APS. Respondents agreed that soldiers managed by the APS reported reduced levels of pain (64.8%) and obtained greater relief (73.9%). The staff generally agreed (73.5%) that the APS had a positive overall impact on patient outcomes.

The Camp Bastion APS also provided opportunities for innovation in dealing with difficult clinical pain situations. For example, ventilator beds within the CSH intensive care unit were limited, and failure to wean patients efficiently from this constrained resource impacted the CSH's mission readiness. Patients who sustained abdominal wounds were notoriously difficult to remove from the ventilator following a laparotomy due to poor respiratory drive secondary to severe abdominal pain. Epidural catheters infusing local anesthetics are a possibility in these patients, although patient positioning and anticoagulation issues often precluded this option. To overcome this clinical dilemma, APS staff employed a bilateral continuous transversus abdominis plane block to provide sufficient abdominal wall analgesia to allow patients to be weaned off ventilator support faster. This was one of the first descriptions of this technique being used within a war theater for this purpose.⁷³

As previously discussed, rapid evacuation of wounded by aircraft has contributed greatly to the increased survival of casualties in recent conflicts. A specific advantage of a functioning APS within the CSH is the ability to prepare patients, from a pain management perspective, for long evacuation flights to medical centers outside the conflict theater.⁷⁴ The use of advanced pain control technology on air evacuation flights, such as patient controlled analgesic infusions, CPNBs, and novel analgesic medications, depends on APS efforts at the CSH for the safe application and transfer of these modalities onto the medically austere aircraft environment. APS services must also be established at the receiving facility for appropriate care plan communication and safe management of pain care modalities at the receiving medical center.

Recognition of the importance of pain management within the roles of care and evacuation chain has resulted in the establishment of a Joint Theater Trauma System Clinical Practice Guideline on Pain, Anxiety and Delirium, most recently updated in March 2017 ([http://jts.amedd.army.mil/assets/docs/cpgs/JTS_Clinical_Practice_Guidelines_\(CPGs\)/Pain_Anxiety_Delirium_13_Mar_2017_ID29.pdf](http://jts.amedd.army.mil/assets/docs/cpgs/JTS_Clinical_Practice_Guidelines_(CPGs)/Pain_Anxiety_Delirium_13_Mar_2017_ID29.pdf)). This document provides a doctrinal basis for the need and establishment of an APS in Role 3 and above medical treatment facilities. It also outlines many of

TABLE 36-1

FREQUENCY OF INTRAVENOUS AND ORAL ANALGESIC ADMINISTRATION

Medication	No. of Patients	Frequency (%) of Patients
Paracetamol (IV)	66	93.0
Diclofenac (IV)	59	83.1
Morphine (IV)	30	42.3
Oramorph SR (PO)	19	26.8
Codeine (PO)	5	7.0
Ketamine (IV)	5	7.0
Ketorolac (IV)	5	7.0
Ibuprofen (PO)	4	5.6
Tramadol (PO)	4	5.6
Acetaminophen (PO)	1	1.4
Amitriptyline (PO)	1	1.4
Co-codamol (PO)	1	1.4
Methocarbamol (PO)	1	1.4

IV: intravenous

PO: per os (by mouth)

Reproduced with permission from: Buckenmaier C III, Mahoney PF, Anton T, Kwon N, Polomano RC. Impact of an acute pain service on pain outcomes with combat-injured soldiers at Camp Bastion, Afghanistan. *Pain Med.* 2012;13:919–926.

the innovations in pain care that have been established during current conflicts. Even with the creation of this wartime practice guideline, organization of APS services in current CSH settings remains inconsistent. General medical command understanding and emphasis of the importance of pain management in combat casualty care is required to make this guideline a standard of practice in the next war.

Roles 4 and 5: Medical Centers Outside the Theater

Role 4 facilities are full-service military hospitals located outside the war theater of operations. LRMC has served as the primary evacuation hospital for both Iraq and Afghanistan and is the current epitome of Role 4 care. The success of new pain technologies established in Role 3 depended on the establishment of an APS presence at LRMC early in the conflicts. During the course of the conflicts, Walter Reed Army Medical

Center anesthesiology residents performed month-long training rotations at the LRMC APS in support of the activity and to gain practical experience in the acute pain management of war casualties. The investment in this training experience by military graduate medical education highlights the importance of the APS activity to casualty management at the critical LRMC casualty evacuation node.

Role 5 military medical centers located within the United States represent the final and most capable expression of military medicine. Recovering wounded remain weeks to months in these rehabilitation facilities, undergoing physical and psychological restoration. The APS service and effective management of pain is, again, a key component of care at this level. Collection of actionable patient-reported outcome data in this complex environment becomes even more critical to provide the needed evidence to drive innovation in pain diagnosis and treatment.

PAIN MEASUREMENT

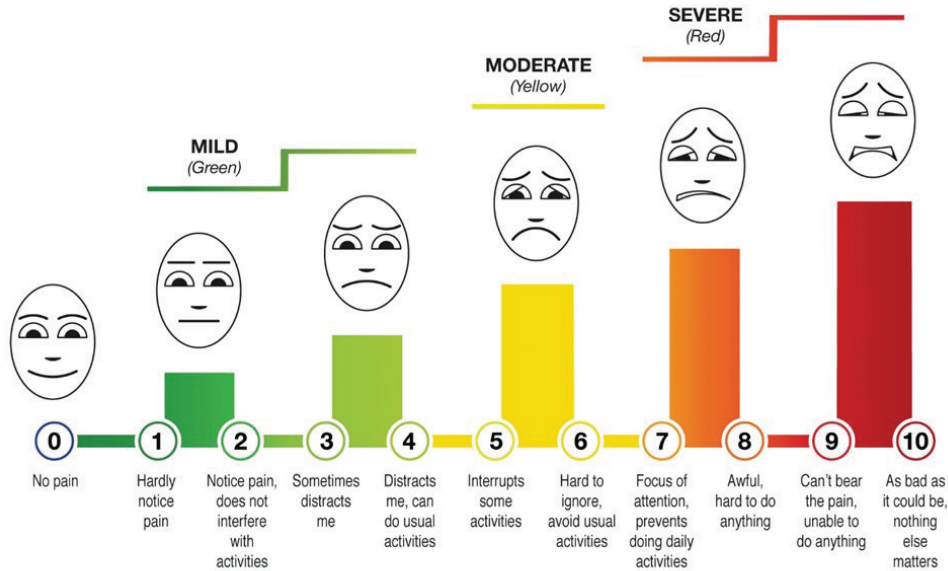
The LRMC APS provided opportunity for some of the only research on casualty pain levels since Beecher's efforts from World War II. A survey of 110 wounded from July 2007 to February 2008 revealed that pain scores in this cohort tended to be high during evacuation flights (>4 on a numeric rating scale), and respondents often failed to receive a 50% reduction in their pain despite recent advances in in-flight pain care.²⁸ Unfortunately, this small survey represents one of the very few attempts to quantify and track casualty pain during the recent years of conflict, representing a missed opportunity to better understand the impact of pain on the recovering casualty. There is a fundamental need for better pain data, collected throughout all roles of care, to enhance the understanding of how pain on the modern battlefield can best be managed to enhance overall patient outcomes.

One of the primary findings and recommendations from the PMTF 2010 report was the need for an improved pain assessment tool able to measure pain intensity, mood, stress, biopsychosocial impact, and functional impact across all roles of care.³⁸ In response, the Defense and Veterans Pain Rating Scale (DVPRS)⁷⁵ was developed and validated to provide a standardized measure for pain in all manner of military treatment facilities (Figure 36-5). The DVPRS scale is unique in its employment of functional language labels for each pain measurement number on the zero-to-ten scale, along with pain faces and colored pain intensity bars to assist patients in rating pain intensity. The use of functional language anchors for each pain intensity number reduces response variability and enhances consistency of the pain question throughout the care

system. The addition of questions on the impact of pain on activity, sleep, mood, and stress emphasizes the important biopsychosocial variables that influence the overall pain experience. Adaptation of the DVPRS as the federal pain question standard through all roles of care could standardize pain data and improve understanding of the clinical impact of pain management treatments. The lack of quality, standardized, patient-reported outcome data on pain has been a major source of inertia in the development and adoption of novel pain care modalities on the modern battlefield. Pain data of this type will become even more vital if the promise of genomics guiding future medical care is to be realized.^{76,77}

The PMTF also recommended the development of a Pain Assessment Screening Tool and Outcomes Registry (PASTOR) to inform clinical care visits and provide comprehensive data on treatment effectiveness. PASTOR utilizes the Patient-Reported Outcomes Measurement Information System (PROMIS) developed through the National Institutes of Health (NIH).⁷⁸ Although a complete discussion of PASTOR is beyond the scope of this chapter, the program leverages computer adaptive technology and validated NIH measurement domains (anxiety, depression, fatigue, sleep impairment, among others) to create a detailed clinician summary report on pain with far more clinically useful information than what is obtained with the standard numeric (0–10) pain rating scale currently used in most clinical situations. Furthermore, this data, along with patient demographic and treatment information, goes into a registry to support process improvement research.

Defense and Veterans Pain Rating Scale



v 2.0

DoD/VA PAIN SUPPLEMENTAL QUESTIONS

For clinicians to evaluate the biopsychosocial impact of pain

1. Circle the one number that describes how, during the past 24 hours, pain has interfered with your usual **ACTIVITY**:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
 Does not interfere Completely interferes

2. Circle the one number that describes how, during the past 24 hours, pain has interfered with your **SLEEP**:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
 Does not interfere Completely interferes

3. Circle the one number that describes how, during the past 24 hours, pain has affected your **MOOD**:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
 Does not affect Completely affects

4. Circle the one number that describes how, during the past 24 hours, pain has contributed to your **STRESS**:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10
 Does not contribute Contributes a great deal

*Reference for pain interference: Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singapore* 23(2): 129-138, 1994.

v 2.0

Figure 36-5. Defense and Veterans Pain Rating Scale.

CONCLUSION

MMOs have a long history of alleviating acute pain and suffering; it is one of the greatest blessings bestowed on the battlefield. Recent focus has been on alternative strategies for acute pain management specific to the various roles of care, branching out

with an expanded armament of medications, as well as nonpharmacologic adjuncts such as RA and acupuncture. The need for the APS system and standardized patient-reported pain outcome data collection cannot be overemphasized as novel medications and

technologies continue to be developed for use in the military environment. There is also a developing understanding about the chronification of pain. The APS system provides a vital link between acute pain care and specialty chronic pain services, which is crucial when chronic pain complicates recovery.

Acute pain chronification is a complex disease process that defies a single medication or procedural solution. Although development of a system approach to pain through the APS may be challenging in the currently taxed medical environment, the elements for establishing APS services are already inherent to deployed and fixed medical facilities. Command emphasis on pain management is required as a key

indicator of patient care quality within all military treatment facilities. This emphasis must be continuously validated through collection of pain care data as patients pass through all roles of care. Investment in this pain care system will establish the infrastructure required to maintain advancements achieved in the present conflicts and stimulate research and innovation in the next conflict. As John Bonica observed in *The Management of Pain*, "The proper management of pain remains, after all, the most important obligation, the main objective, and the crowning achievement of every physician."¹⁰ In the author's own experience, few things in life are as personally rewarding as relieving the pain of a wounded soldier.

REFERENCES

1. Farwell B. *Stonewall: A Biography of General Thomas J. Jackson*. New York, NY: W.W. Norton & Company; 1992: 492–526.
2. Lewy J. The Army disease: drug addiction and the Civil War. *War Hist.* 2013;21:102–119.
3. Brownstein MJ. A brief history of opiates, opioid peptides, and opioid receptors. *Proc Natl Acad Sci U S A.* 1993;90:5391–5393.
4. Ranby J. The nature and treatment of gunshot wounds. In: Van Swieten G, eds. *The Diseases Incident to Armies*. Philadelphia, PA: R. Bell; 1776: 136.
5. Terry CE, Pellens M. *The Opium Problem*. New York, NY: Committee on Drug Addictions and Bureau of Social Hygiene; 1928: 69.
6. Meldrum ML. A capsule history of pain management. *JAMA.* 2003;290:2470–2475.
7. Beecher HK. Pain in men wounded in battle. *Ann Surg.* 1946;123:96–105.
8. Meldrum ML. Brief history of multidisciplinary management of chronic pain, 1900–2000. In: Schatman ME, Campbell A, eds. *Chronic Pain Management: Guidelines for Multidisciplinary Program Development*. New York, NY: Informa Healthcare; 2007: 1–13.
9. Bonica JJ. Organization and function of a multidisciplinary pain clinic. In: Weisenberg M, Tursky B, eds. *Pain*. Boston, MA: Springer; 1976: 11–20.
10. Bonica JJ. *The Management of Pain*. Philadelphia, PA: Lea & Febiger; 1953:593.
11. Apkarian AV, Baliki MN, Farmer MA. Predicting transition to chronic pain. *Curr Opin Neurol.* 2013;26:360–367.
12. Gawande A. Casualties of war—military care for the wounded from Iraq and Afghanistan. *N Engl J Med.* 2004;351:2471–2475.
13. Air transport of the critically injured patient: controlling pain during transport and flight. In: Buckenmaier CC, Bleckner L, eds. *Military Advanced Regional Anesthesia and Analgesia*. Washington, DC: Borden Institute; 2008: 113–118.
14. Buckenmaier CC, McKnight GM, Winkley JV, et al. Continuous peripheral nerve block for battlefield anesthesia and evacuation. *Reg Anesth Pain Med.* 2005;30:202–205.
15. Buckenmaier CC III, Lee EH, Shields CH, Sampson JB, Chiles JH. Regional anesthesia in austere environments. *Reg Anesth Pain Med.* 2003;28 321–327.

16. Owens BD, Kragh Jr JF, Wenke JC, Macaitis J, Wade CE, Holcomb JB. Combat wounds in Operation Iraqi Freedom and Operation Enduring Freedom. *J Trauma*. 2008;64:295–299.
17. Buckenmaier CC 3rd, Bleckner L. *Military Advanced Regional Anesthesia and Analgesia*. Washington, DC: Borden Institute; 2009.
18. Girona RJ, Clark ME, Massengale JP, Walker RL. Pain among veterans of Operations Enduring Freedom and Iraqi Freedom. *Pain Med*. 2006;7:339–343.
19. Woolf CJ. Pain: moving from symptom control toward mechanism-specific pharmacologic management. *Ann Intern Med*. 2004;140:441–451.
20. Ossipov MH, Morimura K, Porreca F. Descending pain modulation and chronification of pain. *Curr Opin Support Palliat Care*. 2014;8:143–151.
21. May A. Chronic pain may change the structure of the brain. *Pain*. 2008;137:7–15.
22. Lew HL, Otis JD, Tun C, Kerns RD, Clark ME, Cifu DX. Prevalence of chronic pain, posttraumatic stress disorder, and persistent postconcussive symptoms in OIF/OEF veterans: polytrauma clinical triad. *J Rehabil Res Dev*. 2009;46:697–702.
23. Rajagopal A, Vassilopoulou-Sellin R, Palmer JL, Kaur G, Bruera E. Symptomatic hypogonadism in male survivors of cancer with chronic exposure to opioids. *Cancer*. 2004; 00:851–858.
24. Raghavan S, Harvey AD, Humble SR. New opioid side effects and implications for long-term therapy. *Trends Anesth Crit Care*. 2011;1:18–21.
25. Angst MS, Clark JD. Opioid-induced hyperalgesia: a qualitative systematic review. *Anesthesiology*. 2006;104:570–587.
26. Sharpe Potter J, Bebartha VS, Marino EN, Ramos RG, Turner BJ. Pain management and opioid risk mitigation in the military. *Mil Med*. 2014;179:553–558.
27. Weisberg DF, Becker WC, Fiellin DA, Stannard C. Prescription opioid misuse in the United States and the United Kingdom: Cautionary lessons. *Int J Drug Policy*. 2014;25:1124–1130.
28. Buckenmaier CC III, Rupprecht C, McKnight G, et al. Pain following battlefield injury and evacuation: a survey of 110 casualties from the wars in Iraq and Afghanistan. *Pain Med*. 2009;10:1487–1496.
29. Upp J, Kent M, Tighe PJ. The evolution and practice of acute pain medicine. *Pain Med*. 2013;14:124–144.
30. Rosero EB, Joshi GP. Preemptive, preventive, multimodal analgesia: what do they really mean? *Plast Reconstr Surg*. 2014;134:85S–93S.
31. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology*. 2012;116:248–273.
32. Ballantyne JC, Carr DB, deFerranti S, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. *Anesth Analg*. 1998;86:598–612.
33. Carr DB, Goudas LC. Acute pain. *Lancet*. 1999;353:2051–2058.
34. Gilron I, Kehlet H: Prevention of chronic pain after surgery: new insights for future research and patient care. *Can J Anaesth*. 2014;61:101–111.
35. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet*. 2006;367:1618–1625.
36. Wu CL, Raja SN. Treatment of acute postoperative pain. *Lancet*. 2011;377(9784):2215–2225.

37. Buchheit T, Van de Ven T, Shaw A. Epigenetics and the transition from acute to chronic pain. *Pain Med.* 2012;13:1474–1490.
38. *Pain Management Task Force Final Report, May 2010.* Falls Church, VA: Office of the Army Surgeon General; 2010.
39. Roles of Medical Care (United States). In: Cubano MA, Lenhart MK, Bailey JA, eds. *Emergency War Surgery.* 4th ed. Fort Sam Houston, TX: Borden Institute; 2013: Chap 2.
40. Deuster PA, Silverman MN. Physical fitness: a pathway to health and resilience. *US Army Med Dep J.* 2013;24–35.
41. Buckenmaier CC. Basic medical skills: pain assessment and control. In: Farr WD, ed. *Special Operations Forces Medical Handbook.* 2nd ed. Washington, DC: US Government Printing Office; 2008: 8-33–8-36.
42. Black IH, McManus J. Pain management in current combat operations. *Prehosp Emerg Care.* 2009;13:223–227.
43. Hinz B, Brune K. Paracetamol and cyclooxygenase inhibition: is there a cause for concern? *Ann Rheum Dis.* 2012;71:20–25.
44. Rinder HM, Tracey JB, Souhrada M, Wang C, Gagnier RP, Wood CC. Effects of meloxicam on platelet function in healthy adults: a randomized, double-blind, placebo-controlled trial. *J Clin Pharmacol.* 2002;2:881–886.
45. Kotwal RS, O'Connor KC, Johnson TR, Mosely DS, Meyer DE, Holcomb JB. A novel pain management strategy for combat casualty care. *Ann Emerg Med.* 2004;44:121–127.
46. US Army. *Combat Medic Field Reference.* Burlington, MA: Jones & Bartlett Learning; 2005.
47. Wedmore IS, Kotwal RS, McManus JG, et al. Safety and efficacy of oral transmucosal fentanyl citrate for prehospital pain control on the battlefield. *J Trauma Acute Care Surg.* 2012;73:S490–S495.
48. White PF, Way WL, Trevor AJ. Ketamine—its pharmacology and therapeutic uses. *Anesthesiology.* 1982;56:119–136.
49. Subramaniam K, Subramaniam B, Steinbrook RA. Ketamine as adjuvant analgesic to opioids: a quantitative and qualitative systematic review. *Anesth Analg.* 2004;99:482–495.
50. Woolf CJ, Thompson SW. The induction and maintenance of central sensitization is dependent on N-methyl-D-aspartic acid receptor activation; implications for the treatment of post-injury pain hypersensitivity states. *Pain.* 1991;44:293–299.
51. Haas DA, Harper DG. Ketamine: a review of its pharmacologic properties and use in ambulatory anesthesia. *Anesth Prog.* 1992;39:61.
52. Green SM, Li J. Ketamine in adults: what emergency physicians need to know about patient selection and emergence reactions. *Acad Emerg Med.* 2000;7:278–281.
53. Schmid RL, Sandler AN, Katz J. Use and efficacy of low-dose ketamine in the management of acute postoperative pain: a review of current techniques and outcomes. *Pain.* 1999;82:111–125.
54. Eastridge BJ, Mabry RL, Seguin P, et al. Death on the battlefield (2001-2011): implications for the future of combat casualty care. *J Trauma Acute Care Surg.* 2012;73:S431–S437.
55. Bonanno FG. Ketamine in war/tropical surgery (a final tribute to the racemic mixture). *Injury.* 2002;33:323–327.
56. Shackelford SA, Fowler M, Schultz K, et al. Prehospital pain medication use by US Forces in Afghanistan. *Mil Med.* 2015;180:304–309.
57. Gaydos SJ, Kelley AM, Grandizio CM, Athy JR, Walters PL. Comparison of the effects of ketamine and morphine on performance of representative military tasks. *J Emerg Med.* 2015;48:313–324.
58. Carr DB, Goudas LC, Denman WT, et al. Safety and efficacy of intranasal ketamine for the treatment of breakthrough pain in patients with chronic pain: a randomized, double-blind, placebo-controlled, crossover study. *Pain.* 2004;108:17–27.

59. Butler FK, Kotwal RS, Buckenmaier CC 3rd, et al. A triple-option analgesia plan for tactical combat casualty care: TCCC guidelines change 13-04. *J Spec Oper Med.* 2014;14:13–25.
60. Petz LN, Tyner S, Barnard E, et al. Prehospital and en route analgesic use in the combat setting: a prospectively designed, multicenter, observational study. *Mil Med.* 2015;180:14–18.
61. Hooper TJ, Nadler R, Badloe J, Butler FK, Glassberg E. Implementation and execution of military forward resuscitation programs. *Shock.* 2014;41:90–97.
62. Koffman RL. Downrange acupuncture. *Med Acupunct.* 2011;23:215–218.
63. Spira A. Acupuncture: a useful tool for health care in an operational medicine environment. *Mil Med.* 2008;173:629–634.
64. Belard JL, Pock AR. Acupuncture and NATO. *Med Acupunct.* 2011;23:271–273.
65. Edwards E, Louis Belard J, Glowa J, Khalsa P, Weber W, Huntley K. DoD-NCCAM/NIH workshop on acupuncture for treatment of acute pain. *J Altern Complement Med.* 2013;19:266–279.
66. Pock AR. Acupuncture in the US armed forces: a brief history and review of current educational approaches. *Med Acupunct.* 2011;23:205–208.
67. Bart-Knauer B, Friedl KE. When will acupuncture become a first-line treatment for acute pain management? *Mil Med.* 2013;178:827–828.
68. King HC, Hickey AH, Connelly C. Auricular acupuncture: a brief introduction for military providers. *Mil Med.* 2013;178:867–874.
69. Gallagher RM, Polomano R. Early, continuous, and restorative pain management in injured soldiers: the challenge ahead. *Pain Med.* 2006;7:284–286.
70. Joshi GP, Ogunnaike BO. Consequences of inadequate postoperative pain relief and chronic persistent postoperative pain. *Anesthesiol Clin North America.* 2005;23:21–36.
71. Buckenmaier C III, Mahoney PF, Anton T, Kwon N, Polomano RC. Impact of an acute pain service on pain outcomes with combat-injured soldiers at Camp Bastion, Afghanistan. *Pain Med.* 2012;13:919–926.
72. Polomano RC, Chisholm E, Anton TM, Kwon N, Mahoney PF, Buckenmaier C III. A survey of military health professionals' perceptions of an acute pain service at Camp Bastion, Afghanistan. *Pain Med.* 2012;13:927–936.
73. Allcock E, Spencer E, Frazer R, Applegate G, Buckenmaier C III. Continuous transversus abdominis plane (TAP) block catheters in a combat surgical environment. *Pain Med.* 2010;11:1426–1429.
74. Baker BC, Buckenmaier C, Narine N, Compeggie ME, Brand GJ, Mongan PD. Battlefield anesthesia: advances in patient care and pain management. *Anesthesiol Clin.* 2007;25:131–145,x.
75. Buckenmaier CC, Galloway KT, Polomano RC, McDuffie M, Kwon N, Gallagher RM. Preliminary validation of the Defense and Veterans Pain Rating Scale (DVPRS) in a military population. *Pain Med.* 2013;14:110–123.
76. Auffray C, Chen Z, Hood L. Systems medicine: the future of medical genomics and healthcare. *Genome Med.* 2009;1:2.
77. McGuire AL, Cho MK, McGuire SE, Caulfield T. Medicine. The future of personal genomics. *Science.* 2007;317:1687.
78. Cook KF, Buckenmaier C 3rd, Gershon RC. PASTOR/PROMIS pain outcomes system: what does it mean to pain specialists? *Pain Manag.* 2014;4:277–283.

