The field of peripheral nerve neurosurgery, as it exists today, developed largely from the knowledge and experience military physicians garnered from wartime injuries sustained by soldiers. The advancement of weapons technology, specifically in the American Civil War and World War I, in tandem with modern medical treatments to improve the survival of soldiers following catastrophic blast-related and penetrating injuries, has led to significant advancements in our understanding of peripheral nerve injuries and their respective treatments. Throughout history, military physicians have carefully characterized the injury pattern of soldiers and described their symptoms, which has helped to advance the classification of peripheral nerve conditions. Based on these observations, military physicians have also attempted different treatments for disorders encountered on the battlefield, efforts that have improved our understanding of the pathophysiology of war injuries and also led to the introduction of broader treatment options for soldiers and civilians.

Causalgia, officially known as complex regional pain syndrome type II, is a pain syndrome characterized by severe burning pain, motor and sensory dysfunction, and changes in skin color and temperature sensation distal to an injured peripheral nerve. The pain syndrome primarily tends to affect combat soldiers after they sustain wartime injuries from blasts and gunshot wounds. Here, the authors provide a historical narrative that showcases the critical contributions of military physicians to our understanding of causalgia and to the field of peripheral nerve neurosurgery as a whole.

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The Origins of Causalgia

Although peripheral nerve neurosurgery has developed significantly in the setting of modern wartime discoveries, the conditions leading to the necessity for such surgery have existed for millennia. With reports dating back to as early as the 11th century, CRPS has a long history intertwined with warfare and traumatic injury. Sayyed Ismail ibn Husayn Gorgani (1040–1136 CE), a prominent Persian physician of the 11th century, also known as Jorjani, mentioned instances of traumatic nerve injury following bloodletting that were common in medieval Persia.4,5 The first documented instance of what was likely CRPS type I, however, was reported by Amboise Paré (1510–1590), an esteemed French barber surgeon of the 16th century who is now also deemed the father of modern surgery. A Huguenot who rose through the ranks of the military amid rampant political tensions and hostility from the Catholic majority, Paré went on to serve as the personal physician for four different French monarchs, including King Charles IX (1550–1574).
In one excerpt, “Chapter XXXVIII. Of the cure of wounds of the nervous parts,” from Paré’s collection of works, he describes being called to evaluate the persistent burning pain that King Charles IX experienced in his arm following a phlebotomy to treat a fever: “he by chance had pricked a nerve [instead] of a vein, the King cried out, that he felt a mighty pain in that place . . . behold the arm began to swell with much contraction, that he could not bend it, nor put it forth.” Paré treated the wound in a manner similar to that used when he famously treated the open wounds of soldiers on the battlefield: with turpentine, oil of roses, and egg yolk. Paré documented the wrapping of King Charles IX’s arm “in a double linen cloth dipped in oxycrate,” a mixture of water and vinegar, and for 3 months Paré applied ointments of “turpentine warmed and mixed with aqua vita,” a liquor, to the wound, after which the king’s injury was “perfectly healed.”

It is believed that Paré’s account may be the first description of CRPS type I. While we now recognize CRPS type I and type II as two distinct entities due to their different precipitating etiologies, it is important to recognize that the efforts of military surgeons like Paré laid the foundations for the field of peripheral nerve neurosurgery in the coming centuries.

In 1813, Dr. Alexander Denmark, a military surgeon of the British Navy who worked at the Haslar Hospital, was the first to specifically document a case of causalgia. A soldier had sustained a gunshot injury at the storming of Badajoz in the Peninsular War and subsequently developed a “violent” and “burning” pain in the median nerve distribution, with palmer ulcerations. Interestingly, Denmark’s written account referenced a radial nerve injury but with a clear description of median nerve pathology. In his surgical exploration of the injured nerve, Denmark discovered that the nerve seemed discolored, “blended,” “intimately attached,” “thickened to twice its natural diameter,” and “with a ball firmly embedded in it.” Denmark suggested resection of the radial nerve, but the patient insisted on a full amputation, after which he experienced a complete resolution of his symptoms.

The American Civil War

It was only during the American Civil War that Dr. Silas Weir Mitchell (1829–1914), now considered to be the father of neurology, expanded Dr. Alexander Denmark’s characterization of causalgia into an official, truly recognized framework of the pain syndrome. In *Gunshot Wounds, and Other Injuries of Nerves*, Mitchell, along with Drs. George R. Morehouse and William W. Keen at Turner Lane’s Hospital in North Philadelphia, cataloged the stories of many soldiers who developed severe burning pain following nerve injuries sustained primarily in the Battle of Gettysburg. One such example was of an 18-year-old man who sustained a gunshot wound that entered “one inch above the sternal end of the [right] clavicle,” avoided the traversing vasculature, and exited in the right posterior arm. The authors reported that the patient initially lost all motor and sensory function in the arm with eventual return of “feeble power.” His “joints became swollen,” his arms became “bent at a right angle,” and his wrist looked as though it was “molded to the curve of the chest on which it lay.” Then, on the “10th day,” the patient experienced severe “burning pain” along his palm and fingers that peaked at 1 month when he also suffered from “loud sounds, vibrations, and dry contact” that then grew slightly less but was subsequently “unaltered.” Even contact of his rubber boots on the floor precipitated the pain, for which the patient prophylactically “wet his stockings.”

Another case documented by the trio of surgeons was of a healthy 27-year-old man who sustained a gunshot wound to his right thigh in Tennessee in 1862. He experienced “prickling pains” “above and inside the knee” that initially worsened, then abated at 2 months, but then the pain subsequently returned and “altered in its character” into a “jagging, shooting, and darting pain” exacerbated by movement. The authors reported that after 2 years, the pain was still refractory to all “ordinary means of treatment” and that while “narcotic infections” initially helped, the patient never experienced continued relief. Mitchell was known for coining the term “phantom limb” to describe patients who experienced significant pain seeming to come from limbs that were already amputated, and in 1867 he coined the term “causalgia,” which combines the Greek words for heat (kausos) and pain (algos), for painful neural injury. Mitchell also described treatments with morphine injected into the affected soft tissue, and like Paré, Mitchell described applications of water-soaked dressing to limbs with burning pain. In a separate book published in 1872, *Injuries of Nerves and Their Consequences*, Mitchell made the now infamous proclamation regarding this pain syndrome, that it was the “most terrible of all the tortures which a nerve wound may inflict.”

The Early 20th Century and World War I

Dr. Paul Sudeck (1866–1945), a German surgeon, expounded on the bony atrophy associated with causalgia in 1900. In his writings, he described the use of “x-rays” to demonstrate osteopenia in patients with causalgia, which Sudeck described as “an inflammatory irritation, which involves nutritional problems … and in consequence resorption of bone” from a variety of conditions, including acute inflammation, fractures, and nerve injuries. Sudeck’s student, Max Nonne, later named the condition “Sudeck’s atrophy,” after his teacher, despite Sudeck’s desire to the contrary.

Following the onset of World War I, American military hospitals filled with patients with peripheral nerve injuries. In 1920, Lieutenant Colonel Charles Frazier reported that there were hundreds of American soldiers with peripheral nerve damage, largely from devastating artillery injuries, in American hospitals. Patients suffered from septic wounds that were not closed and were frequently irrigated with antiseptic solutions. This irrigation reduced overall mortality but resulted in prolonged hospitalization to monitor healing. The nerves in these patients were mangled and sheared, and the patients’ long-term outcomes were complicated by recurrent infections, especially in the absence of antibiotics. It is unclear what the true incidence of causalgia was in soldiers who experienced pe-
Peripheral nerve injuries in World War I, but it likely ranged between 1.3% and 13.8%.\(^17\)

In 1916, Dr. René Leriche (1879–1955), a French military surgeon in World War I, performed the first documented therapeutic periarterial sympathectomy for a patient with causalgia.\(^18\) Leriche had a keen interest in the connection between the sympathetic nervous system and the development of many disorders, including pain. The first patient who underwent the procedure performed by Leriche had suffered from chronic hand numbness and pain after a gunshot wound to the axilla. Leriche speculated that patients suffering from causalgia had symptoms similar to those of patients with ischemic limbs. While Leriche’s premise that an arterial injury produced causalgia was inaccurate, his successful sympathectomy did provide further evidence for a role of the sympathetic nervous system involvement in causalgia.

**World War II**

Despite the continued medical advancements of the 20th century, the wartime experience of World War II unfortunately did not result in any new curative measures for causalgia at any US military hospitals.\(^19\) At Percy Jones General Hospital in Battle Creek, Michigan, artificial fever therapy was attempted in 5 patients with causalgia and was unsuccessful. In Kennedy General Hospital in Memphis, Tennessee, all trials attempting neurolysis of the affected nerves were failures. Although one patient experienced success following repeated injection of papaverine hydrochloride along the distribution of the affected nerve, the success was not reproducible in other patients. With other treatments clearly failing, the focus was placed on “prompt sympathectomy,” as risks associated with surgery were known to be significantly less than those associated with “delayed treatment” of causalgia.\(^19\) While neuromyosis was unsuccessful in most patients with causalgia, if the nerve lesion was “sufficiently severe,” the substitution of sympathectomy for this option was noted to have positive outcomes. Injections of procaine in sympathetic blocks to patients allowed for preoperative assessment of efficacy of sympathectomy, and in some patients even led to cure.

The broad experience that peripheral nerve surgeons gained in World War II led to a clear categorization of peripheral nerve injuries and established an appropriate time course for surgical intervention. The field of peripheral nerve neurosurgery was propelled by the advancement of antibiotics, the introduction of new metallic suture materials that could be radiographically identified to facilitate postoperative assessment of suture lines, and the development of novel nerve grafting techniques. A meta-analysis of the published cases of causalgia during World War II revealed that most soldiers experienced excellent results following sympathectomy.\(^17\) Alongside postwar developments in intraoperative neuromonitoring, medical management of combat soldiers was also further optimized.\(^20\) These advances likely had significant impacts on limiting the progression of causalgia with earlier recognition of peripheral nerve injuries and earlier surgical intervention. Much of the reduction in cases of causalgia over time likely arose from the increased efficiency of medical units regarding triaging, communication, and evacuation technology. This may be why the rates of causalgia were lower following the Vietnam War than after World War II. However, because of the various reporting methods and classifications of causalgia that existed at the time, it is difficult to ascertain whether there truly has been a reduction in rates of causalgia.\(^21\)

**Post–World War II Developments and Recent Wars**

Shortly after World War II, Dr. James Evans, an American physician of the Lahey Clinic, engendered the term “reflex sympathetic dystrophy” for the condition that was previously termed causalgia and demonstrated the therapeutic efficacy of sympathetic blocks on a wider scale and suggested that the likely etiology of causalgia was excessive efferent sympathetic fiber activity.\(^22\) The clinical descriptions put forward by Dr. Evans identified significant heterogeneity for the possible precipitating event for reflex sympathetic dystrophy, including arthritis, sprains, and vascular complications, and became the basis for the description of CRPS type I, in which a clear nerve injury is not present in some injuries or diseases.

Causalgia has remained a persistent condition and has continued to affect soldiers to this day, including those who have fought in the Global War on Terrorism. These soldiers have experienced blast injuries from rocket-propelled grenades, car bombs, land mines, and gunshot wounds. A review of soldiers who served in Operation Iraqi Freedom and were managed in pain clinics found the incidence of causalgia to be approximately 4.3%.\(^23\) The reduction of blast-related pain syndromes among military personnel may be related to the efficacy of modern military triaging protocols used since the Vietnam War. These protocols involve the use of powerful regional anesthesia on the battlefield, during evacuation, and upon arrival to combat support hospitals.\(^24\) Epidural and plexus blocks can allow injured soldiers to achieve longer-acting pain control and prevent pain sensitization.\(^25\) These methods enable optimization of soldiers in nonurgent trials with sympathetic blocks, which, if therapeutic, would be an indication for a sympathectomy.\(^26\) In addition, neuromodulation and stimulation have recently been hypothesized to be beneficial in soldiers with long-term suffering from CRPS or causalgia, and additional research is needed to assess the efficacy of these interventions.\(^27\) Although evidence suggests that interventions like sympathetic blocks and sympathectomies are clearly therapeutic in patients with CRPS type II, this approach may not be effective in the treatment of CRPS type I patients.\(^28\)

**Conclusions**

Military physicians and neurosurgeons have contributed significantly to our understanding of causalgia, first observed as a war injury, and to the field of peripheral nerve neurosurgery as a whole. Improved medical management, regional anesthesia, sympathetic blocks, and surgical sympathectomies may have reduced the incidence of causalgia among combat soldiers, but the pain syndrome still con-
continues to affect the quality of life among combat soldiers long after their initial peripheral nerve injuries. Additional research is needed to elucidate the etiology of CRPS type II among active-duty military personnel and veterans and to generate newer, more efficacious treatments.

References


42. Department of the Army. *Army Techniques Publication ATP 4-02.5: Casualty Care.* 2013.


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