Complex Regional Pain Syndrome of the Upper Extremity

Ryan W. Patterson, MD, MPH, Zhongyu Li, MD, PhD, Beth P. Smith, PhD, Thomas L. Smith, PhD, L. Andrew Koman, MD

The diagnosis and management of complex regional pain syndrome is often challenging. Early diagnosis and intervention improve outcomes in most patients; however, some patients will progress regardless of intervention. Multidisciplinary management facilitates care in complex cases. The onset of signs and symptoms may be obvious or insidious; temporal delay is a frequent occurrence. Difficulty sleeping, pain unresponsive to narcotics, swelling, stiffness, and hypersensitivity are harbingers of onset. Multimodal treatment with hand therapy, sympatholytic drugs, and stress loading may be augmented with anesthesia blocks. If the dystrophic symptoms are controllable by medications and a nociceptive focus or nerve derangement is correctable, surgery is an appropriate alternative. Chronic sequelae of contracture may also be addressed surgically in patients with controllable sympathetically maintained pain. (J Hand Surg 2011;36A:1553–1562. Copyright © 2011 by the American Society for Surgery of the Hand. All rights reserved.)

Key words Chronic pain, complex regional pain syndrome, management, reflex sympathetic dystrophy, upper extremity.

After trauma or surgery, physiologic events and adaptations that contribute to pain (alldynia, hyperpathia, and cold sensitivity), dystrophic events, or impaired function are common. The abnormal prolongation or persistence of these events with persistent pain, cold sensitivity, autonomic dysfunction, microvascular abnormality, localized atrophy, and functional impairment constitutes complex regional pain syndrome (CRPS, also known as reflex sympathetic dystrophy and algodystrophy). Complex regional pain syndrome increases injury or surgical symptoms, delays recovery, and may compound morbidity by secondary complicating events such as arthrosis and delayed healing. Complex regional pain syndrome can increase permanent impairment and strain the physician–patient relationship.

The purposes of this review were to define the subjective and objective manifestations of CRPS, to outline diagnostic criteria, discuss nonoperative and operative treatment options, elucidate common myths and misconceptions, and delineate standard-of-care issues.

DEFINITIONS

Complex regional pain syndrome is a clinical entity without a single pathognomic test or marker. Although multiple synonyms exist, the most common are reflex sympathetic dystrophy, causalgia, and algodystrophy (Table 1).

Based on the recommendation from the International Association for the Study of Pain, complex regional pain syndrome type 1 entails pain syndrome, autonomic dysfunction, trophic changes, and functional impairment without an identifiable peripheral nerve component. This entity corresponds to traditional reflex sympathetic dystrophy. Complex regional pain syndrome type 2 includes the above and identifiable nerve involvement (classic causalgia). The lessening of symptoms and clinical improvement after sympatholytic intervention...
is defined as sympathetically maintained pain (SMP). Failure of improvement after sympatholytic intervention including pharmacologic intervention or sympathetic blocks is termed sympathetically independent pain. Pain may be nociceptive or neuropathic. The former denotes a mechanical or inflammatory process that serves as a constant or intermittent source of pain initiation. “Neuropathic pain” refers to pain related to peripheral nerve irritation or excitability from compression, neuroma, neuroma-in-continuity, or inflammation. If this pain spreads beyond the normal distribution of the involved nerve and is associated with autonomic changes, trophic events, and functional impairment, CRPS type 2 is defined.

WHY YOU SHOULD CARE
Postinjury and postoperative outcomes are negatively affected by CRPS. The recovery course is prolonged, complications are frequent, rehabilitation is impaired, stiffness is common, functional results are inferior, time to return to work is increased, litigation is increased, and patient satisfaction is compromised. Patients with poor outcomes and CRPS may be litigious. Furthermore, plaintiffs with CRPS who prevail in court have increased monetary rewards. An understanding of the clinical subtleties and manifestations of CRPS are crucial in improving patient outcomes and decreasing liability. In patients with persistent pain and refractory symptoms—especially stiffness—CRPS should be in the differential diagnosis, and that deliberation, positive or negative, should be recorded.

Incidence/prevalence
The incidence and prevalence of CRPS are unknown; however, its incidence is higher in smokers versus non-smokers and it occurs 3 to 4 times more often in women than in men. In Olmsted County, Minnesota, the incidence was reported as 5.5 per 100,000 and the prevalence as 20.7 per 100,000 in 2003. The incidence after fracture of the distal radius varies from 4% to 39% in prospective series and may occur after carpal tunnel release with or without iatrogenic damage.

Anatomy and physiology of pain
Pain with cellular damage initiated in the periphery may be from mechanical, thermal, chemical, and ischemic events. Pain signals, potentiated by local reflexes and humeral factors, are relayed via peripheral nerves to the dorsal horn of the spinal cord (wide dynamic range neurons), where they may be amplified and modified and then transmitted to cortical centers. The magnitude of pain depends on the mechanisms of initiating events, afferent information transmitted, efferent modulation, and central nervous system interpretation (Fig. 1). Painful (nociceptive) information is activated peripherally by mechanical, thermal, chemical, and ischemic events and transmitted by small myelinated (Aδ-H) and small unmyelinated C-afferent peripheral nerve fibers to the spinal cord. The perception and physiologic consequences are related to a complex interplay of physiologic events and psychological factors. Complex regional pain syndrome is conceptually an exaggeration or abnormal prolongation of the expected pathophysiologic events after injury or surgery.

Complex regional pain syndrome may result in irreversible end-organ dysfunction, including loss of the normal arteriovenous shunt mechanisms and permanent alterations in central neurologic responses. Ongoing segmental ischemic and cell death may have a substantial role in the process. Swelling and stiffness, and atrophy and contracture may occur and persist. Pain is often associated with arteriovenous shunting and a relative ischemia of the extremity, mechanical events, or nerve irritation.

Natural history
Complex regional pain syndrome types 1 and 2 occur, in part, as a departure from the orderly and predictable

### TABLE 1. Definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>An unpleasant emotional response associated with actual or potential cellular damage</td>
</tr>
<tr>
<td>Analgesia</td>
<td>Absence of pain in response to an insult that should produce pain</td>
</tr>
<tr>
<td>Nociception</td>
<td>Response to an unpleasant (noxious) stimulus that produces pain in human subjects under normal circumstances</td>
</tr>
<tr>
<td>Allodynia</td>
<td>Pain in a specific dermatomal or autonomous distribution associated with light touch to the skin; a stimulus that is not normally painful</td>
</tr>
<tr>
<td>Hyperalgesia</td>
<td>Increased sensitivity to stimulation (includes allodynia and hyperesthesia)</td>
</tr>
<tr>
<td>Hyperesthesia</td>
<td>Increased sensitivity to stimulation (pain on response to a mild nonnoxious stimulus)</td>
</tr>
<tr>
<td>Sympathetic pain</td>
<td>Pain in the presence of or associated with overaction of the sympathetic pain fibers; by definition, the pain is relieved by sympatholytic interventions</td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>Decreased sensitivity to stimulation</td>
</tr>
<tr>
<td>Hyperpathia</td>
<td>Abnormally painful reaction to a stimulus (especially repetitive); often includes extended duration of pain, frequently with a delay</td>
</tr>
<tr>
<td>Dysesthesia</td>
<td>An unpleasant abnormal sensation</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>An abnormal sensation</td>
</tr>
</tbody>
</table>
response of an extremity to a traumatic or surgical insult. The exact pathophysiologic cause is not well defined. A transient dystrophic response with pain, hypersensitivity, and altered autonomic function (abnormal physiology) to injury or trauma is normal. However, an abnormal prolongation of this response and inability of the patient to modulate or control the pain cycle appears to be the best explanation of CRPS. A cascade of reversible and irreversible events may ensue. Because many drugs (pharmaceutical agents) and therapies modify the natural history, it is defined poorly. Dogma states that 80% of those treated within 1 year of injury show considerable subjective and objective improvement, and approximately only 50% of those treated after 1 year improve markedly. However, patients with CRPS after a fracture of the distal radius have a poorer prognosis, with stiffness and “poor finger function” at 3 months being correlated with morbidity at 10 years. Despite early and appropriate treatment, some patients do poorly, with long-term functional impairment, chronic pain, or deformity; arbitrary time frames that do not incorporate pharmacologic, mechanical, and patient activity are not predictive.

**Clinical manifestations and diagnosis**

History, physical examination findings, and diagnostic workup are extremely important. Suspicion that CRPS may be a concern is important, and CRPS should be considered in patients with unexpectedly intense pain, difficulty sleeping, stiffness, slower than anticipated recovery, and no pain relief with narcotics. A history of a surgical or traumatic insult (whether minor or major) is common. Typical pain is described as tearing or burning and is exacerbated often by exposure to cold. Pain is not relieved often or completely by narcotic analgesics and responds frequently to sympatholytic medications. Difficulty sleeping, restlessness, and anxiety are common. On examination, patients may exhibit allodynia (painful response to a nonpainful stimulus), hypehypathria (increased pain sensitivity), and hyperalgasia (increased sensitivity to stimulations). Functional deficits occur owing to pain and swelling, which com-
monly result in stiffness of the fingers, wrist, and shoulder. Trophic changes from autonomic dysfunction include abnormal sweating, swelling, and changes in skin temperature and texture. The involved extremity is either swollen and warm or atrophic and cool. Although women are more frequently affected than men, anyone can be affected. Children and adolescents are afflicted rarely but may manifest with severe involvement. The incidence of upper versus lower extremity involvement is similar. An identifiable mechanical trigger, nerve involvement, or identifiable injury is present in less than 50% of cases.

Diagnostic tests

Plain x-rays may be normal but often show osteoporosis with subchondral and periarticular resorption (Fig. 2). These changes may not be visible for 2 or more weeks after injury. As much as 30% of patients do not have x-ray abnormalities. Bone scans may be characteristic and may help to confirm CRPS but are not pathognomonic. Three-phase scans have been used but are insufficiently sensitive. First- and second-phase bone scans may demonstrate asymmetry of flow dynamics and quantify vasomotor instability and abnormal autonomic flow. When positive, third-phase scans demonstrate increased periarticular uptakes in involved and uninvolved joints. A positive third-phase (bone scan-positive) scan adds credence to the clinical diagnosis and defines a subgroup of CRPS; however, it has limited prognostic importance.9

Thermoregulatory and nutritional blood flow testing permits a qualitative and quantitative assessment of distal-extremity autonomic function. A form of stress (thermal or emotional) improves reliability and reproducibility of this testing. Isolated cold stress testing using both temperature and laser Doppler fluxmetry has been described to assess dynamic sympathetic response of an extremity to changes in environmental temperature. Skin surface temperature is a reflection of total blood flow and laser Doppler evaluates rapid shunting and nutritional flow (Fig. 3). Isolated cold stress testing is sensitive to vasomotor disturbances that occur in 80% to 90% of patients with CRPS; however, it is not specific for CRPS.10 The normal response to cold or alternative stress is predictable and reproducible. In normal subjects, temperature and laser Doppler follow (LDF) parallel response curves. At normal baseline, temperatures will be stable; temperature and LDF will fall during cooling in parallel fashion and will rebound during warming to equal or greater than baseline. In “high-flow” or warm CRPS, temperatures remain elevated during cooling and rebound slightly and vary from digit to digit. Laser Doppler follow characteristically drops randomly compared with baseline and fluctuates during cooling. Both temperature and LDF are increased during warming. In contradistinction, “low-flow” or cool CRPS temperature is low during baseline, cooling, and rewarming, with variation between fingers. Laser Doppler follow follows temperature.

Vital capillaroscopy permits the direct measurement of nutritional blood flow in the nailfold of the hand and foot. Patients with CRPS demonstrate consistently decreased nutritional flow and are unable to modulate flow compared with normal patients. Data from vital capillaroscopy demonstrate decreased nutritional flow in both “warm” and “cool” patients. Decreased nutritional flow also supports irreversible damage to arteriovenous shunts, thereby reducing appropriate nutritional distribution in chronic, longstanding CRPS.

Pseudomotor function may be evaluated by a quantitative and qualitative assessment of sweat production by measuring resting sweat output (RSO). Resting sweat output measures sweat production before or after a sympathetic block; it is primarily a research tool. Quantitative pseudomotor axon reflex correlates highly...
with the RSO. When the RSO and the quantitative pseudomotor axon reflex are combined, consistent differentiation of abnormal autonomic function in patients with CRPS is possible (statistically significant, \( P < .003 \)).

Thermography is an elegant and accurate measurement of temperature. Because it reflects only total flow, inherent limitations are the inability to evaluate vaso-motor and nutritional flow.

Endurance testing is an effective technique to document subtle functional deficits and is performed using computerized equipment. Use of these techniques permits the demonstration of objective signs of weakness and fatigue not possible with the use of static testing. Endurance testing is extremely accurate and difficult to falsify and may demonstrate functional impairment that would otherwise be missed.

**Evaluation of sympathetically maintained pain**

Common diagnostic procedures include stellate ganglion blocks, continuous autonomic plexus blocks, and cervical epidural block. Intravenous phentolamine, which blocks \( \alpha_1 \) and \( \alpha_2 \) receptors, provides a sympatholytic effect and is the reference standard to determine CRPS. Many oral drugs exhibit sympatholytic action. Relief suggests SMP syndrome. Therefore, a positive response (relief of symptoms) supports the diagnosis of CRPS and a negative response (persistent pain) suggests an alternative diagnosis or irreversible peripheral changes with or without central pain. Peripheral nerve conduction velocities and electromyography may be used to identify neuropathic conditions.

**Classification and staging**

Complex regional pain syndrome constitutes a series of reversible and irreversible physiologic events; the time course of these events is determined by the nature of the initiating trauma, inherent physiologic adaptations, and pre-existing comorbidities, therapeutic interventions, and environment episodes. It is crucial to remember that the results of therapeutic intervention may be unanticipated.

Existing classifications do not suggest specific interventions or provide prognostic consequence. Proposed classifications include those of de Takats in 1937\(^1\) and Steinbrocker in 1958.\(^1\) In general, staging based on time is misleading. Because most patients are treated before definitive diagnosis, classifications based on temporal (time in weeks or months) factors are inconsistent and clinically irrelevant.

**Prevention**

A randomized, double-blinded, controlled trial using vitamin C in patients with nonoperatively managed

---

**FIGURE 3:** Isolated cold stress test combining digital temperature and laser Doppler fluxmetry measurements. Digital temperatures are monitored with thermistors attached to each digit of both extremities. Microvascular cutaneous perfusion is assessed with a laser Doppler probe attached to 1 digit of each extremity. Digital temperature and laser Doppler fluxmetry measurements are sampled using custom computer software; the results of the test are plotted for analysis.
wrist fractures demonstrated a lower incidence of CRPS in the vitamin C group (7%) versus the placebo group (22%). Another randomized, placebo-controlled, double-blinded trial found that patients with wrist fractures treated operatively and nonoperatively had a decreased risk of CRPS in the vitamin C groups (overall 2.4%) compared with the placebo group (10.1%). The recommended dose is 500 mg daily for 50 days after injury, as a lower dose of 200 mg daily had an incidence of CRPS of 4.2%, whereas the 500-mg group was 1.8%, which was similar to the 1,500-mg daily group (1.7%). Although claims that vitamin C may reduce the incidence of CRPS after distal radius fractures are controversial, vitamin C has no major morbidity, is inexpensive, and is recommended in the American Academy of Orthopaedic Surgeons Clinical Guideline.

### Treatment

**Treatment**

Treatment or referral for treatment should be initiated on recognition and may be guided by clinical and diagnostic tests to determine the physiologic stage, the presence or absence of sympathetically maintained pain, and the presence or absence of a correctible nociceptive or neuropathic event.

Management options include therapy, vitamins, oral medications, parenteral medications, psychological support, and surgery.

Physiologic staging evaluates the extent of arteriovenous shunting and swelling and may be characterized as high-, normal-, or low-flow states. Patients with high flow states present clinically with a hot, swollen, and painful extremity; increased total flow and inappropriate arteriovenous shunting coincide with ischemic-like pain (burning and tearing). This presentation is often early, rarely has had irreversible events and fixed contracture, is usually sympathetically maintained, and does not respond well to narcotics.

Normal state is the most difficult to diagnose clinically; the hand is not swollen but is painful. Diffuse stiffness, hyperpathia, allodynia, and hyperalgesia are common. Vasomotor tone is abnormal and nutritional flow is low. Narcotics have limited efficacy.

In a low-flow state, the extremity is atrophic and stiff. Pain is diffuse with a tearing or burning quality, vasomotor tone is abnormal, function is impaired severely, and nutritional deprivation exists.

Presence or absence of SMP is determined by improvement or lack thereof in symptoms after sympathetic oral medications, intravenous phentolamine, or autonomic blocks. Sympathetically maintained pain is supported by pain relief after oral sympatholytics (eg, antidepressants and anticonvulsants) with diminution of pain, conversion of diffuse pain to anatomic dermatomes, or distributions. If oral medications are inadequate, Phentolamine or autonomic blocks are used. Although many references suggest stellate blocks as a reference standard, continuous blocks are more reliable and provide more definitive diagnosis, in our experience.

Nociceptive or neuropathic injury or abnormality, if corrected, will often ameliorate symptoms; however, sympatholytic treatment may be necessary to identify mechanical derangements or nerve abnormalities.

### Treatment Sequences

Often multiple modalities are used simultaneously and sequentially. Therapy and oral medications are the first line of treatment. The choice of oral medications may be guided by the physiologic stage, with modification based on patient variability. Except for pregabalin (Lyrica; Pfizer, New York, NY), antidepressants, anticonvulsants, adrenergic agents, and calcium channel blockers are not designated by the Food and Drug Administration for use to treat pain.

The following is provided as a guide to initial pharmacologic and therapy care.

1. High-flow extremities are treated with therapy including contrast baths and stress loading, and a low-dose antidepressant and a low-dose anticonvulsant.
2. Normal flow is treated with therapy including stress loading, contrast baths, and transcutaneous electrical nerve stimulation units, and a low-dose anticonvulsant and a calcium channel blocker.
3. A stiff, painful, cold hand indicates low flow. Therapy consists of active and passive range of motion and a transcutaneous electrical nerve stimulation unit combined with an anticonvulsant and calcium channel blocker.
4. High flow with localized hyperpathia may be treated with a clonidine patch to the hyperpathic area.

These are recommendations for initial care. Other choices are well justified. It is important that the practitioner understands the risks and benefits of these powerful pharmacologic agents, appreciates drug interactions, and monitors the patient carefully. Referral is appropriate at any point of care.

### Psychological management

Psychological pain interventions (especially cognitive behavioral techniques) provide notable pain relief in many chronic pain syndromes. Even though CRPS has not been studied specifically using such interventions, consensus and expert opinion state that these
methods are important adjuncts in the management of CRPS.17

**Therapy**

Therapy and adaptive modalities are combined usually with oral medications. These include hand therapy with active and passive range of motion exercises (within limits of pain), stress loading (scrubbing), splints, contrast baths (alternating heat and cold), and transcutaneous nerve stimulators. A randomized clinical trial demonstrated that functional therapies may improve symptoms in CRPS.18 Another recent controlled trial using 2-point tactile discrimination training while observing a mirror image of the unaffected limb showed significant improvement in both pain and 2-point sensation in the affected extremity.19

**Pharmacologic therapy**

Oral pharmacologic interventions, which provide a sympatholytic effect and improve nutritional flow, are used in the treatment of CRPS. Of note, none are labeled by the Federal Drug Administration for use in CRPS. Multiple classes of drugs are appropriate and include corticosteroids, antidepressants, anticonvulsants, membrane-stabilizing agents, adrenergic agents, and calcium channel blockers (Table 2). Injectable medications may also be used in selected patients.

**Corticosteroids**

Many hand surgeons avoid corticosteroids because of concern about avascular necrosis. However, many medical practitioners consider corticosteroids to be the drug of choice. Evidence suggests a low risk of avascular necrosis with 1 or 2 courses or prednisone or its equivalent. Steroids have efficacy, are inexpensive, and are easily monitored. Increased blood sugar, especially in diabetics, is a concern. Small randomized, controlled trials indicate that a pulse of corticosteroids may improve symptoms in CRPS.20,21

### TABLE 2. Oral Medications

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual Dosage</th>
<th>Mechanism</th>
<th>Major Short-term Disadvantage or Side Effects</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline hydrochloride</td>
<td>25 mg 3 times/d or 50 mg every PM</td>
<td>Inhibits amine pump; decreased norepinephrine uptake</td>
<td>Drowsiness</td>
<td>With guanethidine sulfate</td>
</tr>
<tr>
<td>Gabapentin (Neurontin; Pfizer Inc., New York, NY)</td>
<td>50–200 mg 3 times/d 300–600 mg 3 times/d</td>
<td>Antinociceptive-binding alpha 2-delta subunit Blocks calcium channels Blocks calcium channels</td>
<td>Dizziness Somnolence Peripheral edema Dizziness Peripheral edema Asthenia</td>
<td>Minimal drowsiness</td>
</tr>
<tr>
<td>Fluoxetine (Prozac; Eli Lilly, Indianapolis, IN)</td>
<td>20 mg/day in AM</td>
<td>Serotonin inhibitor</td>
<td></td>
<td>Minimal drowsiness</td>
</tr>
<tr>
<td>Phenytoin (Dilantin; Mylan Pharmaceuticals, Inc., Morgantown, WV)</td>
<td>100 mg 3 times/d</td>
<td>Decreases resting membrane potentials; inhibits amine pump; stabilizes synaptic membrane</td>
<td></td>
<td>Minimal drowsiness</td>
</tr>
<tr>
<td>Fluoxetine (Dibenzyline; WellSpring Pharmaceutical Corporation, Sarasota, FL)</td>
<td>40–120 mg/d</td>
<td>Al-receptor blocking agent</td>
<td>Orthonastic hypertension</td>
<td></td>
</tr>
<tr>
<td>Nifedipine (Procardia; Mylan Pharmaceuticals, Inc., Morgantown, WV)</td>
<td>10 mg 3 times/d; may increase slowly to 30 mg 3 times/d</td>
<td>Ca++ channel blocking agent; prevents arteriovenous shunting; increases nutritional flow</td>
<td>Headache Postural hypotension</td>
<td></td>
</tr>
<tr>
<td>Amlodipine (Norvasc; Mylan Pharmaceuticals, Inc., Morgantown, WV)</td>
<td>5–10 mg every day</td>
<td>Ca++ channel blocking agent; prevents arteriovenous shunting; increases nutritional flow</td>
<td>Headache Postural hypotension</td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>20–80 mg/d; prednisone equivalents × 5–40 d</td>
<td>Stabilize membranes; increase nutritional flow; decrease inflammatory pain</td>
<td>Adrenal suppression; avascular necrosis (dose-related)</td>
<td></td>
</tr>
</tbody>
</table>
Anticonvulsants
Neuroleptics (eg, gabapentin, pregabalin) have mild analgesic effects, sympatholytic actions at a low dose, and efficacy in CRPS.22 The doses used in CRPS are lower than necessary for prevention of seizures. The time course is shorter and the complication profile is acceptable.

Antidepressants
Antidepressants—especially tricyclics—exert a sympatholytic effect and improve nutritional blood flow. Effective doses are generally lower than required for depression. Sedation is common, and for the short-term, often beneficial. Bedtime dosing alone may have efficacy. Tardive dyskinesia is a rare complication.

A meta-analysis indicates that antidepressants are effective in non-CRPS neuropathic pain, with greater efficacy of tricyclics compared with selective-serotonin update inhibitors.23 Although antidepressants have not specifically been tested in CRPS, anecdotally their efficacy has been noted.

Narcotics
Opioids have minimal effect on pain derived from CRPS. A randomized controlled trial in CRPS compared sustained release morphine versus placebo, with no difference in pain over an 8-day period.24

Parenteral medications
N-methyl-D-aspartate (NMDA) blockers: Ketamine has a mechanism of action consisting of NMDA receptor blockade, which has a role in the treatment of severe cases of centrally mediated neuropathic pain, such as CRPS. The NMDA receptor blockade improves the central sensitization component of CRPS, which includes symptoms of allodynia and hyperalgesia. Ketamine produces a state of dissociative anesthesia with amnesia and analgesia. At high doses, side effects include hallucination, erratic behavior, and flashbacks.

There are 3 techniques for ketamine administration: intravenous subanesthetic dosing,25,26 intravenous high-dose anesthesia (“ketamine coma”),27 and topical administration.28

A randomized, placebo-controlled study showed that a 4-day inpatient infusion of subanesthetic ketamine produced markedly greater pain relief than placebo; however, this benefit was lost by week 12 and there was no improvement in function.25 A nonrandomized trial of high-dose intravenous ketamine for 5 days demonstrated substantial pain improvement compared with baseline for 6 months after treatment.27 Without adequate controlled trials, ketamine coma treatment for CRPS should be viewed cautiously. Another double-blinded, placebo-controlled, randomized trial showed that topical ketamine notably reduced allodynia and hyperalgesia.28 Topical ketamine does not elevate serum ketamine levels, and side effects are minimized, thereby allowing potential outpatient use.

Autonomic/sympathetic blockade: Sympathetic blockade is often used in CRPS and has beneficial effects that are short-lived. It provides important diagnostic information with noteworthy improvement in sympathetically maintained CRPS. Furthermore, it allows the physician to perform a more thorough physical examination, potentially finding a nociceptive focus, which may be amenable to surgical intervention.

Invasive treatments
Spinal cord stimulation (SCS) requires the implantation of electrodes in the epidural space and is designed to stimulate the dorsal column at the level of the spinal cord affected by CRPS. A 5-year follow-up of the only randomized, controlled trial using SCS in patients with CRPS demonstrated no statistical difference in pain or quality of life scores in those who received SCS with therapy compared with those who had therapy alone.29 Spinal cord stimulation is costly and invasive and has a relatively high complication rate with minimal benefit at 5 years. Nevertheless, based on multiple case control studies and anecdote, implanted stimulators are used frequently, with repeated efficacy.

Surgical interventions
Surgery may be employed to correct a nociceptive or neurologic initiation of pain in patients with CRPS. Examples include carpal tunnel release after distal radius fracture complicated by carpal tunnel syndrome, neuroma resection or repair, and distal radius malunion or distal radioulnar joint reconstruction. Early surgical treatment of an identifiable pain source is beneficial and risks of CRPS exacerbation are negated by postoperative continuous pain blocks and appropriate oral medications. Multidisciplinary management both preoperatively and postoperatively may improve outcomes with the inclusion of appropriate hand therapy, psychological treatment, and pain management. Hand therapy is particularly important after release of finger contractures, intrinsic contracture, and arthrofibrosis. Typically, extension contractures of the metacarpophalangeal joints and mild flexion contracture of the proximal interphalangeal joints occur; intrinsic muscle–tendon contractures are common. Release of metacarpophalangeal joints has been criticized because long-term improvement averages 50% of intraoperative correction.
However, this improvement has a potential impact on quality of life and function. After release, it is important to evaluate intrinsic resting length. If it is contracted, release of intrinsic contractures enhances grasp and release. Individualized therapy regimens are critical and may include active and passive range of motion, contrast baths, transcutaneous electrical nerve stimulation, fluid therapy, splinting, continuous passive range of motion, and intermittent positive pressure. The goal of therapy should be to minimize swelling, increase range of motion, desensitize the nociceptive focus, and decrease pain.

**MYTHS AND DISINFORMATION**

“CRPS is a psychiatric condition.”
There is abundant evidence to dispute this statement, and its use is pejorative and will cause animosity and ill will. It is not defensible in deposition or trial.

“CRPS spreads though the body.”
“Spread” is rare except on the Internet.

“Surgery is never appropriate.”
Surgery is appropriate in many instances—especially to correct nociceptive and neurologic foci when pain is controlled by pharmacologic interventions.

“The clinical picture is straightforward.”
It is not straightforward; subtle or variant forms of CRPS are common and inadvertent treatment alters the natural history.

**PEARLS OF TREATMENT**

- Recognize that CRPS may be present in patients who have pain that does not respond to narcotics, who have trouble sleeping, and who are stiff.
- Shoulder adhesive capsulitis is common and treatment will improve outcomes.
- Double crush occurs. Evaluate for cervical abnormalities, thoracic outlet, and proximal compression neuropathy.
- Do not rely on courses of stellate blocks. If patients are not improving, request continuous intravenous infusions.
- Use multimodal therapy early with combinations of oral medications and therapy.
- If SMP is controllable with sympatholytic medications, surgery is appropriate.
- Document whether CRPS was considered in all patients with excessive or unexplained pain intensity. Then document again.
- Hand posturing in CRPS, in most, includes metacarpophalangeal extension and proximal interphalangeal in slight flexion or extension. A clenched fist suggests an alternative diagnosis.
- Referral to a pain specialist is appropriate if concern about diagnosis or response to treatment persists.

Complex regional pain syndrome should be considered in any patient with excessive or seemingly inappropriate pain. Suspicion and inclusion of CRPS in the differential diagnosis of unexplained or excessive pain are suggested. Early pharmacologic treatment based on the physiology combined with hand therapy is an appropriate initial treatment. It is appropriate for parenteral management to refer to pain specialists if symptoms and signs persist. Evaluation for surgically correctable problems and surgery under pharmacologic protection is appropriate. Patient-centered care is essential.

**REFERENCES**