

Consensus Report

Complex Regional Pain Syndromes: Guidelines for Therapy

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Abstract:

This report aims to present an orderly approach to the treatment of Chronic Regional Pain Syndrome (CRPS) types I and II through an algorithm. The central theme is functional restoration: a coordinated but progressive approach that introduces each of the treatment modalities needed to achieve both remission and rehabilitation. Reaching objective and measurable rehabilitation goals is an essential element. Specific exercise therapy to reestablish function after musculoskeletal injury is central to this functional restoration. Its application to CRPS is more contingent on varying rates of progress that characterize the restoration of function in patients with CRPS. Also, the various modalities that may be used, including analgesia by pharmacologic means or regional anesthesia or the use of neuromodulation, behavioral management, and the qualitatively different approaches that are unique to the management of children with CRPS, are provided only to facilitate functional improvement in a stepwise but methodical manner. Patients with CRPS need an individual approach that requires extreme flexibility. This distinguishes the management of these conditions from other well-described medical conditions having a known pathophysiology. In particular, the special biopsychosocial factors that are critical to achieving a successful outcome are emphasized. This algorithm is a departure from the contemporary heterogeneous approach to treatment of patients with CRPS. The underlying principles are motivation, mobilization, and desensitization facilitated by the relief of pain and the use of pharmacologic and interventional procedures to treat specific signs and symptoms. Self-management techniques are emphasized, and functional rehabilitation is the key to the success of this algorithm.

Key Words: Complex Regional Pain Syndrome (CRPS) types I and II—Reflex sympathetic dystrophy—Causalgia—Treatment algorithm.

The nature of Chronic Regional Pain Syndrome (CRPS) until recently suffered from a lack of precise definition of what constitutes the disorder, a failure to understand its pathophysiology, and the lack of a mechanism. The epidemiology of CRPS is unknown. Only Sweden, with a population of 8.6 million people, can provide reasonably accurate records that document the incidence of relevant conditions. Causalgia (354E) in 1990 was found in 27 cases; in 1991, in 40 cases; in 1992, in 38 cases; and in 1993, in 29 cases. Reflex sympathetic dystrophy (RSD; 337X) in

1990 was reported in 67 cases; in 1991, in 44 cases; in 1992, in 40 cases; and in 1993, in 80 cases. To put these figures in proportion, the condition described as *pain in an extremity* (729F) was reported in 1990 in 1,249 cases; in 1991 in 1,374 cases; in 1992 in 2,091 cases; and in 1993 in 2,458 cases. These figures are the number of patients who were hospitalized under these main diagnoses and probably represent only the most advanced cases.

It would appear from the foregoing statistics that those conditions referred to as Complex Regional Pain Syndrome represent a constant, small, but significant medical entity. In an attempt to define a taxonomy that more accurately describes conditions that fall under the umbrella term *Complex Regional Pain Syndrome*,¹ the IASP Committee on Taxonomy recently revised its previous descrip-

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tion and published those clinical features consistently found in these conditions.² To satisfy a diagnosis of CRPS type I (RSD), the clinical findings include regional pain, sensory changes (e.g., allodynia), abnormalities of temperature, abnormal sudomotor activity, edema, and an abnormal skin color that occur after a noxious event. CRPS type II (causalgia) includes all of the foregoing features in addition to a peripheral nerve lesion.

Because the pathophysiology of these syndromes is poorly understood and treatment will be directed of necessity to their clinical features, some understanding of what constitutes CRPS is required. The term CRPS was chosen for the following reasons:

- Complex expresses the varied clinical features found in these conditions.
- Regional emphasizes that in the majority of cases it involves a region of the body, usually an extremity, but may occur on another part of the body or spread to different areas of the body.
- Pain is considered essential to the diagnosis of CRPS types I and II and includes pain that is spontaneous or evoked such as allodynia or hyperalgesia. In rare cases otherwise resembling CRPS, pain may be minimal or absent.

Although motor symptoms and signs are not directly included in the classification, tremor, dystonia, and weakness are found in many patients with CRPS. It is also recognized that some patients may not have all of the criteria that will clearly classify them as having CRPS type I or II. The new classification allows for any exceptions that might constitute a third type of CRPS by categorizing them as *not otherwise specified*. The definitions of CRPS types I and II contain exclusion criteria that prevent the inclusion of patients with pain and clinical findings that are temporarily proportionate anatomically and physiologically to an injury. Other conditions that may constitute a myofascial pain syndrome are also excluded. Furthermore, a diagnosis of CRPS would be precluded by the existence of any known pathology that would otherwise account for symptoms and signs present in the distal parts of an extremity but outside of the territory of an injured nerve. These symptoms and findings may also occur within specific innervation, but this is not an absolute requirement. The names *reflex sympathetic dystrophy* and *causalgia* are retained in parentheses in the new classification to facilitate communication and understanding.

DIFFERENTIAL DIAGNOSIS

Although CRPS types I and II typically describe disorders in the distal part of an extremity, pain may occur in a

region such as the face or trunk. For example, pain beyond the site of an initial lesion including changes in skin blood flow, edema, and sudomotor activity in the vicinity of a peripheral or cranial nerve might meet a definition of CRPS type II (causalgia).¹ However, a similar situation might prevail in which the absence of allodynia or hyperalgesia and the lack of vascular changes, sudomotor changes, or edema would prevent a diagnosis of CRPS. Also, many pain dysfunction syndromes that present with some features (e.g., spontaneous pain, edema) but without other vasomotor changes typical of CRPS would not be sufficient to satisfy this diagnosis. Malingering and factitious disease are excluded, although many patients with CRPS type I or II may suffer from psychological or psychiatric disturbances. Neuropathic pain such as sympathetically maintained pain (SMP) that is found in CRPS types I and II is a phenomenon associated with the underlying pathophysiology that in the case of causalgia includes neurologic damage but does not of itself constitute a syndrome or clinical disorder.

Before proposing a coordinated approach to the treatment and management of patients with these syndromes, it is worth reviewing the cardinal symptoms and signs that constitute CRPS.

Pain

Pain generally follows a known initiating noxious event, which at first seems to be physically quite minor. It may also seemingly occur as a result of an immune reaction. The pain is disproportionate in duration, severity, and distribution to that which would be expected in the normal clinical course of the inciting physical event. The noxious event may occur peripherally, in the central nervous system, or in the viscera, or may be a psychological/psychiatric disorder. The pain may be spontaneous, deep, and aching in quality aggravated by orthostasis and touch or solely evoked by either mechanical or thermal stimuli giving rise to allodynia or hyperalgesia.

Vasomotor abnormalities

Swelling occurs in most instances and affects joints and other soft tissues. Eighty percent of CRPS cases have temperature side differences that may be either colder or warmer than the contralateral extremity³ and are associated with changes in skin color.

The vasomotor and sudomotor abnormalities tend to be more obvious early in the course of the disorder.

Trophic changes

Although these are generally described as occurring late in the disorder, they may appear within weeks of its onset. Skin, nail, and hair growth changes are frequently seen. In some cases, allodynia may be so severe that the extremity

ty is held in a protective posture further accelerating the development of trophic changes in both integument and deeper structures.

Motor changes

Weakness, tremor, and reduced movement are frequent accompaniments of CRPS.

What follows is a proposal for a coordinated approach to functional restoration built around a treatment algorithm, and attempts to normalize function should guide CRPS therapy.⁴⁻⁷ The primary philosophy is that medications, analgesics including regional anesthesia, neuromodulation, and psychotherapy are only agents designed to facilitate these goals. This patient population is dysphoric and requires sympathetic understanding and encouragement to achieve objective and measurable rehabilitation goals. The algorithm is the basis for achieving functional improvement by using physical therapy, which in itself is specific and follows principles that have been found to promote function

without exacerbating autonomic dysfunction and symptoms. The algorithm aims at functional improvement by physical therapy at a *measured* pace but is time contingent. Other modalities are added to achieve graded but methodical progress. The dynamic and unique nature of this disease entity must allow for individual flexibility and application of treatment protocols and the variable use of exercise therapy. Only an interdisciplinary team approach is likely to succeed. The biopsychosocial interplay is fundamental to the delivery of treatment of which the patient must become a key member. Self-management is emphasized, and whereas low technological intervention should prevail, regional anesthetic procedures or neuromodulation are recommended if there is any failure to achieve progress. To achieve these goals and develop a physiotherapeutic algorithm, basic scientists and physicians drawn from many disciplines took part in a consensus workshop (Table 1).

PHYSICAL THERAPEUTIC ALGORITHM

Early intervention is paramount, and ideally each step in the algorithm should be accomplished within 2-3 weeks. Chronic or complicated cases may require longer for each step with the proviso that any lack of progression, after 3 weeks, would necessitate more aggressive intervention and psychotherapy. Should a time frame greater than 3 weeks be adopted because of the severity of the disease or psychological difficulty or pathology, the importance of adhering to definitive time lines will still remain. Incremental goals are psychologically advantageous but require substantial attention in support of the patient. Patients who progress more rapidly than 2 weeks per step should be encouraged and allowed to advance within the limits of their symptoms.

The first step primarily involves the development of a therapeutic alliance and rapport. Motivation, mobilization, and desensitization come next. The process of desensitization may involve both a pharmacologic approach to reduce pain and sensitivity and a process of gentle controlled nonnociceptive stimulation using heat, massage, pressure, cold, vibration, movement, etc., to help restore normal sensory processing.

It is essential that movement phobia be overcome and the patient begin to actually move and allow the limbs to be touched (Fig. 1).

To overcome barriers to movement and initiate muscle activity, isometric strengthening and electrode stimulation (if tolerated and salutary) should be explored.⁸ Any secondary myofascial pain syndromes affecting supporting joints should receive treatment.

The third step is made up of isometric strengthening and stress-loading (i.e., scrubbing, walking, and carrying weights).⁹ General aerobic conditioning, especially to consolidate general reactivation, is encouraged.

TABLE 1. Members and their topics of the consensus workshop to develop a physiotherapeutic algorithm

Group	Topic	Participants
I	Exercise-specific therapy and behavioral management of Chronic Regional Pain Syndrome types I and II: role of analgesia	Harold Merskey, Canada P. Prithvi Raj, United States, group leader Angela Mailis, Canada Richard Rauck, United States Elliott Krames, United States Gunnar Olsson, Sweden Edward Covington, United States
II	Novel routes, new agents, and combined pharmacotherapy to facilitate rehabilitation	Samuel Hassenbusch, United States, group leader Michael Cousins, Australia Nelson Hendler, United States Gabor Racz, United States Wen-Hsien Wu, United States Ralf Baron, Germany Donald Price, United States Wilfrid Jänig, Germany Joshua Prager, United States
III	Neuroaugmentation with or without adjunctive pharmacotherapy for rehabilitation or maintenance analgesia	Peter Wilson, United States, group leader Torsten Gordh, Sweden David Niv, Israel Michael Rowbotham, United States John Oakley, United States Robert Wilder, United States
IV	Management of CRPS—Early and late: Development of treatment algorithm	Robert Boas, New Zealand, group leader Norman Harden, United States Michael Stanton-Hicks, United States Christopher Glynn, United Kingdom Giancarlo Barolat, United States Martin Koltzenburg, Germany Nagy Mekhail, United States

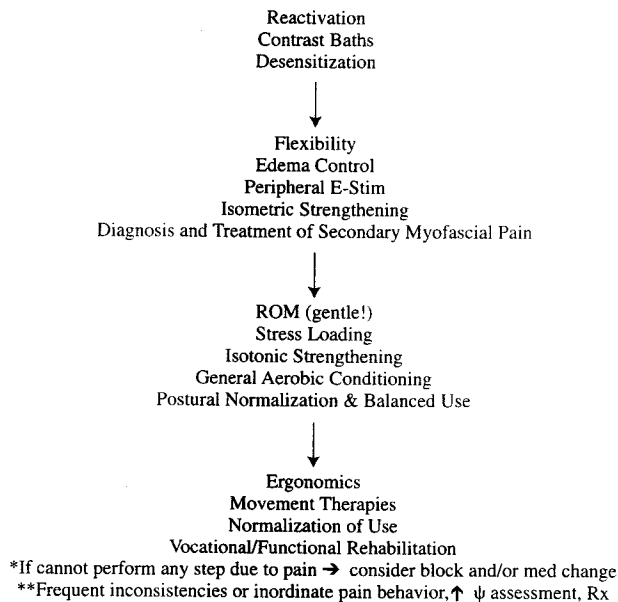


FIG. 1. Compound diagram of the physiotherapeutic algorithm and modalities that are used to achieve movement toward functional restoration. The listing of each modality does not imply a specific order or priority. The use of any intervention is determined by the rate of progress at the time. ROM, range of motion.

Range of motion

It is particularly important to avoid aggressive or passive range of motion (ROM) tests, especially in an extremity that is insensate after regional anesthetic blockade. Maintenance of and a gentle gradual increase in active ROM is the goal. Attention is directed to achieving postural normalization, stabilization, and balanced use of the limbs.

The fourth and last step aims at complete functional recovery. This emphasizes normalization of function in the affected limb. Specific interventions that overcome residual disability are appropriate and include autonomic assessment and intervention, vocational rehabilitation with work hardening, functional capacities evaluation, and written instructions. Modifications are appropriate in adult patients who are working. Return to school, homemaking, or whatever endeavor is appropriate should be specifically facilitated and integrated with a daily occupational therapy and/or therapeutic recreation. Any psychological difficulties or frank psychiatric illness that may be impediments to a patient's progress through the algorithm require standard behavioral management and supportive psychotherapy.^{10,11} A cognitive behavioral approach to pain avoidance, overprotection, movement phobia, and bracing is in order. Depression, anxiety, inappropriate anger, and personality disorders need appropriate full pharmacotherapy and psychotherapy (see Psychological Management).

Where the severity of pain is the main limiting factor in any progress through the algorithm, then aggressive treat-

ment of the nociceptive or neuropathic generator is in order. The use of pharmacologic, regional anesthetic, or neuromodulation techniques is paramount. The best guide to optimal intervention is a clear diagnosis that is identified by history and physical examination with special emphasis on those factors that contribute to disability: role of biological versus psychological/psychiatric versus socioeconomic should be clearly catalogued. The combination of medications, psychotherapeutic interventions, regional anesthetic blocks, and specific physical modalities (i.e., electrostimulation) is selected to allow progression through the algorithm (see Regional Anesthetic Techniques).

Difficulties of treatment

Severe cutaneous allodynia may be a limiting factor and requires specific treatment. An amplified course of cutaneous desensitization requiring progressive use of coarse textures for massage, proprioceptive challenge that include scrubbing, and weight-bearing should be instituted. This will usually require pain relief through sympathectomy (either pharmacologic or regional) or an escalation of analgesic pharmacotherapy or both. Dependent edema is treated by elevation, active ROM, and appropriate anti-edema garments or pumps and diuretics.

The presence of contractures will limit progress through the algorithm.¹² It is essential to examine the extremity, under regional anesthesia or a general anesthetic, to determine the degree of any fixed limitation to joint movement. Only active or very gentle passive manipulation can be done after regional blockade. Analgesia is frequently required for the initial stretching maneuvers with the proviso that the patients determine their own physical limits, thereby avoiding physical injury. Usually frequent gentle work done by the patient will be sufficient, however, sometimes dynamic splinting and serial splinting are used and may be helpful in specific patients. Casting or splinting that results in immobility of the limb is counterproductive and may be contraindicated unless required for stabilization of a fracture or for limited periods of time such as at night. It is critical to progress slowly and within patient defined limits when using these techniques. Adequate and liberal analgesia (pharmacologic or interventional) should be used to facilitate these steps (Fig. 2).

For CRPS in the lower extremities, weight-bearing can be the rate limiting step in the latter stages of the algorithm. For this reason, in such patients, hydrotherapy can be extremely useful. This therapy should proceed through a graduated weight-bearing program. Key therapies at this point are scrub-loading (stress-loading) techniques for the upper extremities and modified scrub-loading (e.g., PABS board) techniques in the lower. In the lower extremities, balanced walking is excellent therapy and should be encour-

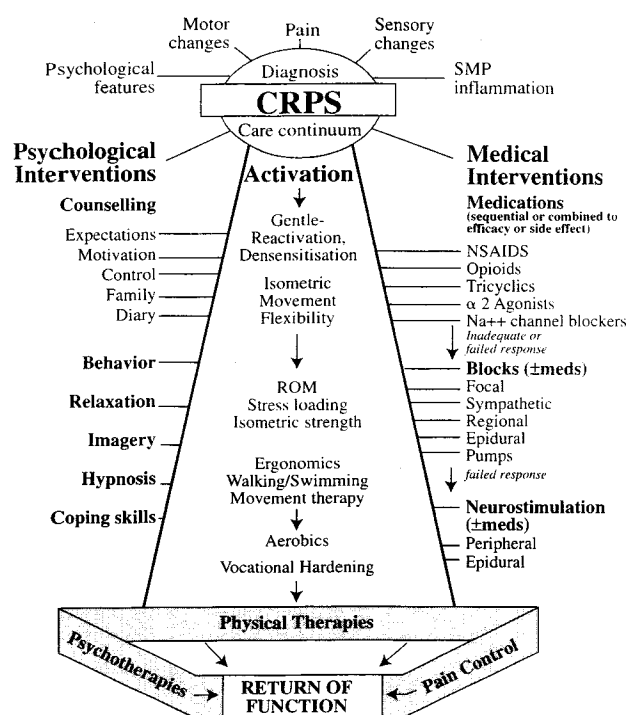


FIG. 2. Essential levels of physical therapy governed by progress that is limited only by the degree of pain and successful treatment of pain by using the different pharmacological or interventional modalities. CRPS, Chronic Regional Pain Syndrome.

aged as much as tolerated. For the upper extremities, weight-bearing using progressively heavier weights is salutary.

When progressing into the last stages of the algorithm, it is important to focus on self-management techniques and where possible to minimize dependence on invasive and technical modalities. As vocational rehabilitation proceeds, the use of those medications that can impair cognition should be limited to facilitate the full participation in vocational opportunities. Careful attention to the continuing need for restrictions and modifications that will ensure vocational success are critical adjuncts to complete reintegration.

PHARMACOLOGIC MANAGEMENT

There are few well-designed treatment trials of neuropathic pain. This is especially the case for CRPS. Most descriptions of CRPS trials are small anecdotal clinical studies with few experimental findings. Without adequate predictors for the choice of therapy, current practice is chaotic and continues to use the "trial-and-error" approach.

What follows is a list of medications that have been found useful, to a greater or lesser degree, in the treatment of CRPS. Their order of presentation does not constitute any form of priority but rather acknowledges the report of their usefulness in managing CRPS.

Nonsteroidal anti-inflammatory drugs (NSAIDs)

NSAIDs and metamizole that irreversibly inhibit cyclooxygenase and therefore reduce production of algogenic substances are worth consideration during the early manifestation or mild stage of CRPS types I and II.¹³ Although pain relief is frequently far from satisfactory, as an adjunct to other therapy particularly where there is joint and tendon involvement in the inflammatory process, their early application is suggested. After reaching what would be considered a therapeutic level with no reduction in symptoms, the drug should be replaced by a second member of the series (e.g., Nabumetone). Because the potential for side effects, particularly renal failure and gastrointestinal ulceration, is high, the risk-benefit ratio must be carefully weighed before persisting with this therapy. The topical use of these drugs is experimental, and their efficacy in children is low.

Opioids

Use of opioids is controversial. Although opioids are considered to be ineffective in neuropathic pain¹⁴ and there has been a reluctance by physicians to use these drugs in nonmalignant pain states, more recent novel studies have demonstrated that they can be extremely useful in selected patients with postherpetic neuralgia or other neuropathic pain syndromes.^{15,16} However, their efficacy varies widely.

No controlled studies of opioid use in CRPS exist. Opioids should be tested early in the course of CRPS types I and II after less potent analgesics have proved to be inadequate, and any trial of therapy should not be delayed to a "last resort" status. An intravenous trial such as by patient-controlled analgesia may be most informative. The earliest application of opioids requires extreme caution in patients who have a history of chemical dependence. Physicians should be aware that their abrupt discontinuation must be avoided. The efficacy of opioids in children with CRPS has not been demonstrated.

Tricyclic and "heterocyclic" antidepressants

The efficacy of some serotonin/norepinephrine reuptake blockers (amitriptyline, desipramine, maprotiline) has been demonstrated in neuropathic pain syndromes such as diabetic neuropathy and postherpetic neuralgia (PHN).¹⁷⁻²¹ The exact mechanism of action of these drugs is not known. All components of neuropathic pain (i.e., spontaneous pain, shooting pain, and allodynia) may be improved. The mean dose that is required for pain reduction may be smaller than that necessary to achieve their antidepressant actions. Some antidepressants demonstrably improve sleep, mood, and anxiety in addition to pain. An individual dose titration, depending on beneficial action and side effects, is important. Selective serotonin reuptake inhibitors (SSRI) are no more effective than placebo in patients who are not

depressed, suggesting that the action of amitriptyline or clomipramine in neuropathic pain depends on an as yet unidentified mechanism. In CRPS, however, SSRI drugs seem to be effective in chronic cases. Until now, however, no controlled studies have been initiated.

Membrane stabilizers

If shooting or paroxysmal pain is present, "membrane-stabilizing," anticonvulsants, local anesthetics, and antiarrhythmic agents may be worth a trial. Controlled studies of these drugs in patients with neuropathic pain are rare. Among the anticonvulsant drugs, carbamazepine and, to some extent, phenytoin or valproic acid are most commonly used in equivalent anticonvulsant dosage.^{22,23} In recent studies, gabapentin, a selective voltage-gated Ca^{2+} channel blocker, has demonstrated some efficacy in the management of pain in CRPS.²⁴

Mexilitine (Boehringer, Ingel, Germany), an oral antiarrhythmic lidocaine analogue, has shown promise for alleviating pain in diabetic neuropathy with a dose of 10 mg/kg.²⁵ The benefits of systemically administered local anesthetics (e.g., intravenous lidocaine, 125 mg/kg) have been reported in postherpetic neuralgia and painful diabetic neuropathy.^{16,26} Intravenous application may predict the response to oral analogues.^{27,28} Transdermal application of lidocaine in a recent blinded study was shown to produce a statistically significant reduction of PHN pain.²⁹

The topical application of local anesthetics [e.g., lidocaine and prilocaine in combination (eutectic mixture of local anesthetic)] is a recent therapeutic alternative for the administration of a local anesthetic for localized neuropathic pain with hyperalgesia or allodynia.²⁹ The value in patients with CRPS has not been determined.

Gamma-aminobutyric acid (GABA) is a widely distributed, primarily inhibitory neurotransmitter. Drugs that interact with GABA transmission (e.g., baclofen) have been reported to alleviate different neuropathic pain conditions, but their use in CRPS has not been studied.

Corticosteroids

Corticosteroids have been advocated in those cases of early CRPS that present with rubor, edema, and heat. Steroids may possibly reduce the inflammatory sequelae of the disease.³⁰ Recent scintigraphic investigations with radiographically labeled immunoglobulins have shown an intraosseous plasma extravasation in patients with CRPS type I that in part combines an inflammatory component in the disorder.³¹ In particular, a trial of corticosteroids is recommended if sympathetic blocks relieve spontaneous pain and have no effect on pain that is due to joint movement and/or trophic changes. The efficacy of steroids has not been confirmed but warrants further investigation.

Calcitonin biophosphonates

Subcutaneous injection of calcitonin has a mild effect on spontaneous pain. No differences in anti-edema efficacy could be demonstrated in a blinded placebo trial.^{32,33} Any analgesic effects should be demonstrated after a few injections, thereby obviating the need for a long therapeutic course over many weeks.

Capsaicin

Topical capsaicin cream previously reported to be efficacious in postherpetic neuralgia and painful diabetic neuropathy is believed to interfere with cutaneous nociceptive C-fiber function.³⁴⁻³⁶ The chronic cutaneous application of capsaicin leads to a reversible depletion of peptides including substance P and calcitonin gene-related peptide from the C-fiber nerve terminals, resulting in activation and subsequent reversal of C-fiber function. Should localized areas of hyperalgesia be present, it may be worth considering a therapeutic trial using concentrations of 0.025–0.075% solutions.³⁷

Adrenergic drugs

Alpha-blockers (terazosin, prazosin, phenoxybenzamine) tend to have little clinical utility but significant cardiovascular side effects.³⁸ Nevertheless, their efficacy has been demonstrated in approximately 30% of patients who dramatically respond to either a trial of phentolamine infusion or the complete relief of symptoms after regional anesthetic sympathectomy. The transdermal application of topical alpha-2 agonists such as clonidine is useful when applied to a discreet area of hyperalgesia.^{39,40} Intraspinal and epidurally administered clonidine has also been shown to relieve pain in CRPS.⁴¹ Beta-adrenergic blockers are generally ineffective.

REGIONAL ANESTHETIC TECHNIQUES

There are two reasons to consider the use of regional anesthetic techniques to facilitate the management of CRPS. The first is the provision of analgesia commensurate with a program of functional restoration. Second, sympathectomy can be provided in those cases that either by phentolamine infusion or regional anesthetic sympathetic block have demonstrated unequivocal evidence of SMP.^{42,43} In the absence of any clinical trial to demonstrate the relative efficacy of somatosensory conduction block with sympathetic blockade, there is a historical preference to use the latter technique regardless of whether the upper or lower extremity is involved. Blocks of the sympathetic nervous system interrupt nociceptor visceral and somatic afferents and vasomotor, sudomotor, and visceromotor fibers.

Once it is established that sympathectomy is effective in relieving not only the burning dysesthesia but also allodynia

or hyperalgesia, it is important to repeat the procedure to determine whether an increasing duration of effect can be expected in any particular patient. If this is the case, these individual blocks may be all that are necessary to enable a patient to regain function by using a specific stress-loading physical therapy. Determining the efficacy of sympatholysis in the upper extremity requires that in addition to the signs of Horner's syndrome (e.g., myosis, ptosis, and enophthalmos), there must be a relief of symptoms and a temperature rise to at least 35°C measured at the finger pulp. In the lower limbs, signs of successful sympatholysis are venodilatation and a temperature $\geq 35^\circ\text{C}$ measured at the great toe pulp. When sympatholysis completely relieves the symptoms and facilitates exercise therapy but is limited in its duration of effect, it is appropriate to consider a prolonged block by using one of the neurolytic techniques. The simplest method is that with a neurolytic agent such as phenol prepared with radiocontrast media such as meglumine (Conray 420, Malingckrodt, St. Louis, MO) or by using radiofrequency lesions. Duration of effect from 3 to 6 months may be achieved, thereby allowing the progress of exercise therapy to continue.

In those countries where guanethidine is available, intravenous regional block can provide alpha-adrenoceptor block for cases in which SMP has been demonstrated.⁴⁴ Although the mechanism of the improvement of symptoms has been questioned,⁴⁵ recent results with this treatment in patients with severe neuralgia have substantiated its efficacy. These investigators demonstrated that allodynia to vibration was completely normalized in responders but not in those cases that had sympathetically independent pain.

Continuous conduction block of the brachial or lumbar plexus can be successfully used for periods of up to 6 weeks.⁴⁶ The main difficulties associated with these techniques are dislodgment of the catheter or infection. However, in those cases that progress rapidly through the steps of the functional algorithm, this level of analgesia may only be needed to accelerate their progress to a point where oral medication will suffice. Central neural infusions into the cervical epidural or lumbar epidural spaces help greatly in managing severe allodynia, pain of joint movement, and continuous pain.

Epidural catheters that are implanted for a long duration should be treated as minor surgical procedures requiring the utmost sterility. This can only be successfully accomplished by using fluoroscopic imaging during their introduction into the ipsilateral epidural space. Instability of the catheter in certain individuals with frequent dislodgment will require the catheter to be surgically retained to paraspinous tissues. Depending on the severity of pain, the long-acting local anesthetic bupivacaine will provide satisfactory analgesia in most cases without any unacceptable proprioceptive or motor effects. These latter side effects may not only be a nuisance but can be frankly incompat-

ible with functional restoration. Therefore, it may be necessary to use an opiate that, together with the local anesthetic, can be adjusted to provide a level of analgesia that is commensurate with exercise therapy demanded at the time. Although fentanyl is one of the most successful opiates for this purpose, untoward side effects may necessitate the use of alternative agents such as morphine, dilaudid, or sufentanil.

A short (2–5 days) hospitalization will be necessary to determine the clinically most effective dose in each case. Once a satisfactory combination of infusion rate and dose of agents is achieved, it also may be necessary to provide the patient with self-dose (bolus) increments at the time of their exercise therapy.

Epidural catheters may be retained for as long as they are required. However, after 6 months of use, consideration should be directed to a trial of neuromodulation using either spinal cord stimulation (SCS) or peripheral nerve stimulation (PNS), whichever modality is considered more appropriate.^{47,48} The practical use of epidural infusions may be limited by considerations such as occupation, repeated infection, and in those cases of lower extremity CRPS in which hydrotherapy is considered the treatment of choice. The main complication associated with continuous epidural infusion is local infection, which is almost invariably superficial to the deep fascia and is therefore treated with systemic antibiotics. It is generally not necessary to remove the catheter, but if paraspinous or spinal infection is suspected, the patient should undergo neurologic examination and magnetic imaging or computed tomography with myelography.

The foregoing regional anesthetic techniques are used to promote the course of functional restoration in conjunction with any other pharmacotherapy that is considered necessary. Regional analgesia will provide an appropriate level of analgesia and sympatholysis for this purpose. Other therapy already discussed may include the use of tricyclic antidepressants, membrane stabilizers (either anticonvulsant or antiarrhythmic), and adrenoceptor antagonists. The alpha-2 adrenoceptor agonist, clonidine, has been found to be particularly useful when administered intraspinally together with a local anesthetic or opiate. The concurrent administration of clonidine will also reduce the dose of local anesthetic and opiate respectively.⁴¹

NEUROMODULATION IN THE TREATMENT OF CRPS

SCS and PNS

Although spinal cord stimulation has been in use since 1967, few investigations have attempted to determine its efficacy in the treatment of specific pain syndromes. Only one paper has prospectively looked at outcome in a small group of patients with CRPS. Several small studies have

reported their retrospective experience with the use of SCS in treatment of pain due to CRPS. Robaina et al.⁴⁹ reviewed eight patients with CRPS involving the upper extremity. Stimulation was applied at the C5-7 region followed by a 10-day trial of a percutaneously externalized electrode. On reevaluation after 27 months of permanent implantation, these investigators reported that 88%, or seven of eight patients, had good to excellent results. Excellent referred to 90–100% pain relief, and good referred to 75% pain relief and only minimal doses of psychotropic agents. Broseta et al.⁵⁰ studied 11 patients who fulfilled the description consistent with a definition of CRPS, including symptoms of intractable burning pain related to a specific nerve injury or amputation and pain localized to either the lower or upper extremities. During the 13-month follow-up, six patients reported excellent relief (i.e., 100% pain free without the need for analgesics and return to work), two patients had continued good relief of pain and one fair results (i.e., 25–75% relief of symptoms without return to work), and two had poor results (i.e., <25% pain relief and still using strong opiate analgesics).

The only other study in the literature is that by Barolat et al.⁵¹ This study described 18 patients with clinical features consistent with CRPS type I (RSD), who were refractory to more conservative intervention. Four of these had no benefit during a 1-week externalized screening trial. Three patients also had no benefit from sympathetic blockade, spinal anesthetics, intrathecal opiates, or intravenous guanethedine. Fourteen patients were subject to permanent implantation of the SCS system. Of these, six reported good pain relief, and five moderate relief of their symptoms. None of the patients was free of pain after the procedures, but three of the six had good relief and were able to discontinue their use of opiates, whereas the remaining three had a significant reduction in their opiate requirements. A mixed series of patients that included CRPS type I (RSD) and CRPS type II (causalgia) studied by Sanchez Ladezma et al.⁵² provided the following results. Eight of the 11 CRPS type I (73%) had sufficient relief of their symptoms to justify implantation, whereas 11 of 13 CRPS type II patients had implantation. The value of this study lies in the long follow-up period of 5.5 years in which 89% still reported excellent relief (75–100% pain relief) and 10% reported good pain relief (50–70% pain relief). The only outcome study describing the use of PNS in treatment of long-standing CRPS⁵³ demonstrated good to fair efficacy in 63% of the 32 patients studied.

Twenty percent of those previously unemployed or employed part time returned to work, and all patients in the successfully treated group no longer required strong analgesics. Although selection criteria are paramount when evaluating modalities such as SCS and PNS, it is apparent that almost 70% of properly selected patients with CRPS

types I and II will in fact respond sufficiently to permit their participation in the treatment algorithm. It should be emphasized, however, that neuromodulation is but one tool that provides both analgesia and sympatholysis to facilitate functional restoration after all other modalities have failed. In some cases of vocational necessity, it may be necessary to provide this level of analgesia and sympatholysis by neuromodulation as the first rung of the physiotherapeutic algorithm. In these instances [e.g., a police officer with CRPS type II (causalgia) who continues to work], the patient would satisfy these criteria and at the same time be an unsuitable candidate for an infusion system.

CRPS IN CHILDREN

CRPS is found in children, adolescents, and adults.^{54,55} CRPS in children, although essentially carrying the same clinical features, demonstrates some important differences from CRPS in the adult and is much more responsive to conservative treatment.^{8,56–58} Children are more likely to respond favorably to a single regional or sympathetic block. Only a few require the intensity and scope of treatment frequently needed in the case of the adult.

However, a very small percentage of children do develop a severe debilitating form of the disease requiring progression along the treatment algorithm described in the present study.^{55,59} Like adults, the initial treatment for children should be physical therapy. This may be difficult to initiate because they may have already been told not to do any exercises that will cause pain in the limb. This advice is often given by well-meaning health care providers who are unfamiliar with CRPS. Simply stating that children should endure a progressive desensitization and exercise therapy program may be sufficient if commenced early in the disease. However, it is necessary to educate the patient and the family of the nonprotective nature of neuropathic pain in CRPS.

Many children will have already received some type of physical therapy before the diagnosis has been made. This may sensitize the children into not accepting additional physical therapy simply because "it doesn't help" or because it is overly painful. The addition of analgesics may overcome these objections. Transcutaneous electrical nerve stimulation (TENS) will frequently afford adequate analgesia in more than half of pediatric patients with CRPS.⁵⁵ In these patients, TENS may suffice to provide all of the needed analgesia with virtually no side effects. Useful medications include nonsteroidal anti-inflammatory drugs, tricyclic antidepressants, and anticonvulsants. These are administered with strict attention to the possibility and degree of any side effects. Given the potential need for treatment over many weeks or months, those medications having the least noxious side-effect profile are desirable. Similarly, the choice of tricyclic antidepressants will

depend on the side-effect profile and one that suits the needs of the patient. Amitriptyline is the most effective in the patient who is unable to sleep at night, although desipramine, with less anticholinergic side effects, may be preferable in those patients who have little difficulty in sleeping and who are unable to tolerate those medications that are more sedating.

The use of cognitive, behavioral, and psychological strategies is particularly germane for pediatric patients with CRPS.^{54,55} These approaches assist in not only the control of pain but help the child to manage the stress of the condition. Psychological counseling may also be necessary to encourage those families to cope with the effects of their child's condition. A high degree of family dysfunction is associated with this disorder.⁶⁰ In a small number of cases, a noninvasive approach will be inadequate to provide the level of pain relief commensurate with their physical therapy. These children may benefit from sympathetic nerve block. It may be preferable to use a catheter technique rather than repeated single shots. A greater percentage of children with CRPS of the lower than of the upper extremity will need a lumbar sympathetic block. Because this is uncomfortable, it is appropriate to use sedation, and the procedure requires the accuracy provided by fluoroscopy. The use of a lumbar sympathetic catheter will avoid the need for repeated procedures. Although the lumbar sympathetic catheter may provide a more specific block for exercise therapy, it is more likely than an epidural catheter to become dislodged. In either case, the maximum benefit of regional anesthesia will only be achieved if physical rehabilitation and behavioral therapies are undertaken while the infusion is running.

It is rare for more invasive treatment of CRPS in children to be required. There are also few data that suggest which course is more correct for those children who have failed the foregoing strategies. Given the proviso that it is preferable to use the least invasive and most reversible modality, a spinal cord stimulator in rare cases should be preferable to a PNS simply because of the ease of placement, the simplicity of a percutaneous trial, and the subsequent ease of removal should it no longer be required at a later date. As a last resort, after all efforts have failed and one has reached the bottom of the treatment algorithm, a neurodestructive technique such as sympathectomy should be considered for those patients with impending tissue loss, edema, recurrent infection, or ischemic necrosis. In those instances, a chemical or radiofrequency lesion is preferable to surgical sympathectomy. It should be remembered, however, that, although immediate benefit may be realized, long-lasting pain relief is rarely obtained.

In summary, the treatment of CRPS in children should commence use with the least invasive measures and progress to more invasive techniques only when conservative thera-

py fails. More than half of these patients will respond to physical therapy in combination with TENS, cognitive and behavioral management, and the possible use of oral medication. The use of early sympathetic block in children is usually not needed. It is rarely required, it increases medical costs unnecessarily, and it perpetuates the mistaken idea that CRPS may be cured by absolving the patient of responsibility for progressing through the physiotherapeutic algorithm.

PSYCHIATRIC AND PSYCHOLOGICAL MEASURES

Whereas a number of diseases, such as ileitis, colitis, chronic back pain, temporomandibular pain syndromes, vaginal pain, and even CRPS, have been associated with patient personality profiles, most of the studies that have attempted to show this correlation with a particular disease or disorder fail to address the problem from a longitudinal perspective⁶¹⁻⁶⁴ and are subject to problems of selection bias. Thus, the physician is faced with a critical problem:

1. Did the disease cause the psychological problem?
2. Do predisposing psychological problems facilitate the expression of complaints that may or may not have a physical basis?
3. Has the patient developed psychological illness as a result of pain and disability?

In one study, of 76% of patients who had both chronic pain and depression, only 11% with premonitory depression consulted with a psychiatrist.⁶⁵ Psychological evaluation of this issue depends on knowing the patient's premonitory condition, history of prior painful illness,^{66,67} and the influence (or lack of influence) of prior painful illness or any current independent sources of distress for the patient.^{65,68-71} It also depends on deciding if there is adequate evidence in support of a relevant psychiatric diagnosis.⁷²

In most cases, onset of pain would be defined as the precipitating event, and objective clinical features would be found consistent with a diagnosis of CRPS supported by temperature side differences using thermometry or passive infrared thermography and cold-pressor testing, X-ray appearances, quantitative sweat testing, and quantitative sensory testing.

Earlier in the disease (0-2 months), no psychological counseling is needed because no psychological changes have yet appeared and the patient expects to get well. Psychological instruments including the MMPI, the Suicide Risk Test,⁷³ the Beck Inventory, and the SCL-90 are all normal, except for some increase in scores in scales 1-3 of the MMPI and similar scores in the SCL-90.

From 2 to 6 months, however, patients become anxious and concerned about why they are not getting well. There

is now a new focus on organic pathology. The MMPI shows further elevations in scales 1 and 3, the Suicide Risk Test is usually normal, the Beck Inventory shows mild depression, and the SCL-90 demonstrates anxiety and depression. In addition to progression through the algorithm, treatment requires confirmation of the diagnosis, the need for patient advocacy, and the need to educate the patient about the disease once the diagnosis is confirmed. The integration of patient care is now essential, and the use of low-dose antidepressants for anxiety and pain with normalization of diurnal rhythms is indicated. Biofeedback for relaxation, temperature control, and the reduction of muscle tension are indicated.

Beyond 6 months, all patients demonstrate varying degrees of depression, the result of chronic pain, disturbed sleep, and anxiety because the disease is not improving. The Suicide Risk Test is usually normal, but because there is a 10 times higher chance of suicide in chronic pain patients if this test is abnormal, psychiatric hospitalization is indicated. The Beck Inventory begins to show moderate to severe depression and the SCL-90 has elevated states of depression, hostility, somatization, anxiety, and interpersonal sensitivity. If not already established, treatment consists of becoming the patient's advocate, identifying the diagnosis, and providing continued support and education regarding the disease. At this stage, antidepressants are required in higher doses, but a single antidepressant at an adequate dosage level is preferable to the combination of different antidepressants. Amitriptyline may be preferable to the newer SSRIs. Biofeedback for relaxation, temperature control, and reduction in muscle tension are indicated. Group therapy with other chronic pain patients, the spouse, or family is now useful as is family counseling. The use of strong opiates such as slow-release morphine (MS Contin, Roxane, Columbus, OH) or methadone is controversial at this stage. In the late stages of CRPS (8 years or longer), patients become less depressed, are resigned to their disease, and do not expect to return to their former vocation. Sleep disturbances are still present together with some anxiety and depression. The MMPI shows elevated scales 1 and 3. This can be wrongly interpreted as a conversion reaction. The Suicide Risk Test is usually normal, the Beck Inventory shows mild to moderate depression, and the SCL-90 has elevated states of hostility, "somatization," anxiety, and interpersonal sensitivity. Treatment is directed to assisting the patient to adjust to a new lower set of life goals. Antidepressants and sedatives are indicated. Education regarding the disease process goes a long way to reduce anxiety associated with the problem and helps to strengthen the patient's own defenses against the consequences of the disease. Group therapy with other chronic pain patients, with the spouse or family in attendance, is particularly useful.

The McGill-Melzack pain questionnaire is a useful tool along with the visual analogue scale or verbal digital scale

TABLE 2. Visual psychiatric treatment algorithm for Chronic Regional Pain Syndrome

1. Onset of pain [go to 2].
2. If pain is treated—STOP. If pain persists more than 2 months, [go to 3].
3. Administer BDI, SRT, HARS, or other preferred short psychological evaluation [go to 4].
4. If any of the tests in [3] are abnormal, [go to 5]. If all tests are normal, [go to 6].
5. Institute appropriate psychotherapy [go to 7].
6. Institute low-dose antidepressants and [go to 7].
7. If pain persists longer than 6 months, [go to 8].
8. Administer MMPQ [go to 9].
9. If the MMPQ shows that the patient is objective, [go to 10]. If the MMPQ shows that the patient is exaggerating, [go to 11].
10. Increase antidepressants, readminister the BDI, HARS, or alternative, SCL-90, and SRT [go to 12].
11. Readminister the BDI, SCL-90, and SRT [go to 13].
12. Institute group therapy, seek psychological review, biofeedback, and anti-anxiety medication if SRT is abnormal; consider psychiatric hospitalization [go to 14].
13. Focus on psychotherapy, not medical treatment, unless there is compelling medical evidence for continued medical care [go to 14].
14. Ongoing psychiatric support until the patient is stable and then STOP.

BDI, Beck Depression Inventory; SRT, Suicide Risk Test; HARS, Hospital Anxiety and Depression Scale⁷⁴; MMPQ, McGill-Melzack Pain Questionnaire.

not only to measure the severity of pain but also to track the progress of treatment. Psychological interventions for patients with reactive depression from chronic pain are numerous, but the efficacy of group therapy and education regarding the disease process are probably as effective as any adjuncts to facilitate progression through the algorithm of functional restoration (Table 2).

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