

# INTERVENTIONAL THERAPIES

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“Levels of evidence” used in this section:

Level 1: Meta-analysis or systematic reviews.

Level 2: One or more well-powered, randomized, controlled trials.

Level 3: Retrospective studies, open label trials, pilot studies.

Level 4: Anecdotes, case reports, clinical experience, etc.

## THE ROLE OF INTERVENTIONAL THERAPIES IN THE TREATMENT OF CRPS

Interventional therapies, including nerve blocks, drug infusions, and implantable pain treatment devices have all been advocated for the treatment of complex regional pain syndrome (CRPS).<sup>1</sup> This section will present information about the role of each block or technique individually and present an algorithm for a “best practices” utilization of these procedures to treat CRPS, citing the best available evidence where available.

As the mechanisms of CRPS are better understood, mechanistic based treatments should be forthcoming; but in the meanwhile, different interventional and noninterventional treatment modalities are applied empirically in a timely manner to facilitate reanimation of the affected extremity. In this section, the historical basis and evidence for the use of nerve blocks in the treatment of CRPS will be reviewed. There have been several topical reviews/meta-analysis articles on this topic and they will be included. Individual studies will be included periodically for several reasons: to highlight a good quality study, to note a novel (or newer) treatment, or to highlight some aspects of clinical decision-making. Blocks included in this section include: sympathetic nerve blocks (SNB), intravenous regional techniques (IVRA), intravenous (IV) infusions, “other” blocks (including somatic and spinal infusions), neurolytic sympathetic blockade, and implantable therapies (including neurostimulators and intrathecal pumps).

## SYMPATHETIC NERVE BLOCKS

Over time, much research and clinical experience has provided evidence that CRPS is a posttraumatic painful neurologic and inflammatory syndrome involving the somatosensory, sympathetic, and often the somatomotor systems.<sup>2</sup> This evolution of mechanistic thinking reveals a complex condition which consists of local inflammation (and perhaps neurogenic inflammation) out of proportion to injury, severe pain in the skin, subcutaneous tissues, and joints, evidence of central hyperexcitability, and sympathetic dysfunction and asymmetry (which represents a logical target for injection therapy).<sup>3</sup> The sympathetic nerve block (SNB) has been recognized as an important procedure both in the diagnosis and treatment of CRPS, with ablative surgical techniques described back to the 1940s or earlier.<sup>4</sup> Historically, the nomenclature Reflex Sympathetic Dystrophy (RSD) implied mechanistic involvement of the sympathetic nervous system, which led to the belief that the diagnosis of RSD could be confirmed with a positive clinical response to sympathetic blockade.<sup>5</sup> With growing evidence and new diagnostic criteria,

utilizing SNB for diagnostic purposes is no longer warranted. However, in the subgroup of CRPS with sympathetically maintained pain (SMP), there is considerable evidence of coupling of sympathetic nerves with several types of afferent nerve fiber types in the peripheral and central nervous system.<sup>6</sup>

Blockade of the sympathetic nervous system is traditionally accomplished at the level of the stellate ganglion (SGB) or lumbar sympathetic (LSB) chain, depending on the location of the painful syndrome (upper versus lower extremity, respectively). The pain relief following SNB generally outlasts the effects of the local anesthetic, and may be long-lasting in some cases.<sup>7,8</sup> In addition to these anatomic local anesthetic blocks, other sympatholytic procedures, including intravenous (IV) phentolamine, IVRA with either lidocaine, bretylium, clonidine, reserpine, or guanethidine, and epidural infusion (for sympathetic blockade) have been described.<sup>9-13</sup> The role of the sympathetic block has been called into question, yet most treatment algorithms still consider at least one sympathetic block (or infusion of sympatholytic agents) necessary to classify CRPS as SMP or sympathetically independent pain (SIP), but again, not for diagnostic purposes.<sup>14,15</sup> There is considerable difficulty in “clinically assessing” the successful sympathetic block, and many “clinically successful” blocks provide a varying degree of sympatholysis.<sup>16</sup> Thus, the role of this block is in the realm of practical treatments based on traditional patterns. With a new understanding of CRPS as including both SIP and SMP, and the realization that it is clinically difficult to assess the degree of sympathectomy provided by SNB, the role of these blocks in a treatment algorithm is largely empiric (lack of a solid evidence base), but clinically important in individual cases as far as it facilitates amelioration of pain and can improve functional outcomes, and thus can provide a less painful “window of opportunity” for rehabilitation techniques.<sup>16</sup>

A systematic review by Cepeda et al was published in 2002 that reviewed all available literature regarding local anesthetic sympathetic nerve blockade from 1916 through 1999.<sup>17</sup> They screened 79 reports of which 50 were rejected due to small sample size, lack of validated or methodical assessments, or undisclosed CRPS patient selection details. The remaining 29 studies were evaluated in detail. These included 19 retrospective reports, 5 prospective case series, 2 nonrandomized controlled studies, and 3 randomized control trials (RCTs)(one in abstract form, see Table 1). For multiple reasons, including evolving diagnostic criterion for CRPS and the recent increase in the sophistication of pain and functional assessment tools, these older reports tend to be relatively imprecise and performed on heterogeneous/nonspecific cohorts. Sixteen of the studies quantified the magnitude of response (see Table 1). Overall conclusions are limited due to the lack of rigorous evidence; in fact it may be erroneous to pool any of this data (as shown in Table 1), due to the extreme variability of the reports.

Another significant confounding factor in assessing the efficacy of SNB is lack of consensus on defining the criterion of a successful sympathetic block. There are several studies available to clarify relevant issues. Price et al did an interesting study of local anesthetic versus saline stellate ganglion or lumbar sympathetic blocks in seven CRPS patients in a double-blind crossover fashion.<sup>7</sup> Onset of analgesic effect occurred within 30 minutes in *both* groups, with the local anesthetic group (lidocaine/bupivacaine mixture) having a significantly greater duration (mean of 3 d 18 h versus 19 h),<sup>7</sup> thus showing at least short-term analgesic efficacy of local anesthetic sympathetic blockade for CRPS (level 2 evidence). Bonelli et al did a randomized trial of stellate ganglion block versus “active control” [in the form of guanethidine IV regional block — actually another treatment, so not really an “active control”].<sup>18</sup> They found significant improvement in both groups, with no significant difference between the SGB and IVRA guanethidine groups (level 3 evidence).

Raja et al undertook a blinded prospective trial of IV phentolamine infusion versus local anesthetic sympathetic blockade in 20 patients (10 upper and 10 lower extremity SMP patients). They found a high correlation between analgesia with SNB and IV phentolamine infusion and concluded that either technique could distinguish between SMP and SIP (see <sup>19</sup>; level 2 evidence).

Malmqvist et al defined strict sympathetic block success criterion [(4 out of 5 equals success: (1) Horner's syndrome; (2) increase in skin temperature >34C; (3) increased skin blood flow >50% by laser Doppler flowmetry; (4) abolished skin resistance response ulnar; and (5) abolished skin resistance response radial)] in an observational study of 54 stellate ganglion blocks. Only 15 of 54 blocks met this strict criterion for a successful block<sup>20</sup> — thus indicating the relatively high rate of partial or incomplete sympathetic blockade clinically. Less than 20% of the articles reviewed by Cepeda critically evaluated the success of their blocks.<sup>17</sup> Schurmann et al showed the clinical difficulty regarding correlation of limb temperature elevation, Horner's syndrome, and complete sympathetic block as measured by an elegant, complex experimental design in a large group of CRPS type I patients.<sup>16</sup> This study clearly showed that even in the case of significant limb temperature elevation, the sympatholysis may be incomplete, with the same holding true for the Horner's syndrome. Additionally, even in patients with a complete sympatholysis, the rate of analgesia obtained following the stellate ganglion block was a little higher than 50%, clearly demonstrating subgroups of SIP and SMP within this group of 33 CRPS type I patients.

To summarize, there is some (albeit limited level 2) evidence for the efficacy of the classic SGB and LSB in select CRPS patients with SMP, but the main reason to perform these blocks is to differentiate SMP from SIP — realizing the clinical interpretive difficulty of a “successful” block as outlined above. If the block provides good analgesia in a patient, then a short series of blocks in conjunction with active reactivation physiotherapy is advocated based on consensus recommendations.<sup>1</sup>

#### IV REGIONAL ANESTHETIC BLOCKS (IVRA)

IV regional anesthesia has been used for years to empirically treat CRPS.<sup>21</sup> Numerous IVRA medications, alone and in combination, have been reported to have efficacy in treating CRPS. IVRA with guanethidine, lidocaine, bretylium, clonidine, droperidol, ketanserin, or reserpine have been described and reviewed critically by Perez et al, Forouzanfar et al, and Kingery.<sup>22-24</sup>

Perez et al undertook a meta-analysis of the highest quality (blinded, with re-evaluation of included trials, statistical methodology; and inclusion only of trials meeting strict inclusion criterion such as randomization, blinding, sample size, drop out rate, and others), finding 11 acceptable trials of “sympathetic suppressors,” nine being IVRA studies and six concerning guanethidine in particular.<sup>22</sup> Perez et al applied a quantitative analysis of effect size which compares the difference in pain relief between experimental and control groups, with a correction factor applied for trial size. This method has become acceptable in meta-analysis to analyze aggregate treatment effect from numerous studies. Their aggregate analysis showed lack of proven effect of IVRA and lack of proven effect more specifically of guanethidine IVRA (thus level 1 evidence for lack of proven effect of these therapies).

Several good quality studies have also reported a negative outcome of the IVRA intervention (no better than placebo). Ramamurthy et al<sup>25</sup> did a double-blind, crossover, controlled outcome study with 60 CRPS I patients randomized to receive IVRA blocks every 4 days for a total of four blocks with either guanethidine (one, two, or four guanethidine blocks) or placebo in 0.5% lidocaine. After the first block, placebo response was higher than guanethidine, and 6 months after the last block (up to four), 35% of patients had significant pain relief, without difference between placebo and guanethidine arms (level 2 evidence for lack of effect of guanethidine over placebo).<sup>25</sup> Confounding factors in this study include the fact that the “placebo” group received an IVRA using local anesthetic (0.5% lidocaine) and a tourniquet — which may confer some type of analgesic effect following the block; thus in reality, the “placebo” control is an active treatment comparison group.

Jadad used an enriched trial design, and prospectively enrolled patients who reported pain relief with open label guanethidine IVRA to a double-blind treatment phase with crossover design. No differences between guanethidine and placebo were seen, and this study was terminated early for side effects (level 2 evidence for *lack of effect*).<sup>26</sup> Blanchard et al compared the effects of IVRA with guanethidine versus reserpine versus saline (placebo arm). This was a crossover design, changing to another agent if inadequate analgesia occurred with a block. Only 21 patients were studied, but no differences between treatment types were discernable at short-term follow-up.<sup>12</sup> The placebo saline infusion is done with a tourniquet in similar fashion to the active drug block; thus, this does not control for a tourniquet-induced effect on the extremity (eg, tourniquet-induced analgesia, compression-induced alteration of local cytokines) leading to methodological problems with the “control” group for most IVRA studies.<sup>23</sup> Rocco et al did a small randomized, double-blind, active controlled trial of reserpine and guanethidine (at different times) versus lidocaine alone in IVRA.<sup>27</sup> They noted significant relief following the block with no difference between the reserpine, guanethidine, or “control” (lidocaine) group.

The notable exception to these negative trials was Hord et al, who found a positive response with bretylium in a prospective randomized double blind fashion versus lidocaine (level 2 evidence).<sup>10</sup> Bonelli et al compared IVRA guanethidine to SGB in a cohort of 19 “RSD” patients<sup>18</sup> and demonstrated “comparable efficacy.” Guanethidine and bretylium have been increasingly unavailable in the United States and guanethidine has largely fallen out of favor.

Clonidine is an alpha-2 agonist that possesses analgesic properties in topical and epidural usage. Reuben and Sklar reported a small case series of the use of IV regional clonidine (1 mcg/kg) in combination with 0.5% lidocaine to treat seven consecutive patients with lower extremity CRPS.<sup>11</sup> They selected patients who responded to one LSB to participate in a prospective, open label study. Near total pain resolution was obtained in 5/7 patients with a short series of clonidine IVRA blocks (two to four blocks), with a lengthening period of analgesia after each block. The two nonresponders were found to have ongoing knee pathology at reoperation. No significant side effects were seen (level 3 evidence for a positive effect with IVRA clonidine).

Some advocate combination drug IVRA to optimize synergistic medication effects across medication classes. The rationale for this approach is theoretically sound, although the evidence is lacking. The combination of IVRA bretylium, phentolamine, and hydrocortisone has had a favorable case series reported in abstract form (level 4 evidence).<sup>28</sup> Other groups have advocated an IVRA lidocaine with ketorolac combination in a small case series (level 4 evidence).<sup>29</sup>

To summarize, the IVRA technique is a procedure that allows placement of medications directly into the affected extremity. Again, efficacy is difficult to assess based on the available literature, with most of the guanethidine trials failing to show improvement in efficacy of guanethidine over lidocaine. There is lower quality evidence available to support the use of other agents — including bretylium, phentolamine, clonidine, lidocaine, and ketorolac — alone and in combinations. Ultimately, as our understanding of the peripheral alterations in cytokines is clarified, this technique may allow targeted pharmacotherapy to the affected limb.<sup>30</sup>

## IV INFUSIONS

A phentolamine infusion has been postulated as a test for SMP. This short acting alpha-adrenergic blocking agent needs to be given by infusion. Arner reported a critical analysis of the use of phentolamine infusion, followed by IVRA guanethidine to assess clinical response to: (1) the phentolamine infusion and (2) to assess the positive predictive value of the phentolamine infusion on a subsequent IVRA guanethidine block's success.<sup>9</sup> Arner divided the results into causalgia and RSD adults versus causalgia and RSD children. In adults, Arner found that approximately 50% obtained markedly positive analgesia with IVRA phentolamine infusion and a complete correlation to an excellent response to guanethidine. In children, 37/47 obtained markedly positive analgesia to phentolamine infusion and a very strong correlation to an excellent response to IVRA guanethidine (32/37 excellent response). Arner concluded that phentolamine caused no complications, and provided “diagnostic” information as to the presence of SMP and prognostic information about subsequent response to guanethidine (level 3 evidence for IV phenolamine).<sup>9</sup> A major weakness of the Arner study was the lack of a control or placebo group. By contrast, Verdugo et al found that neither placebo, phentolamine, nor phenylephrine infusions gave any significant changes in pain, QST testing, regional blood flow, nor hyperalgesia — with no difference between groups in a prospective, single-blinded, nonrandomized study (level 3 evidence for *lack* of effect of phentolamine).<sup>31</sup>

A critical evaluation of IV infusion of lidocaine was undertaken by Wallace et al in a randomized, double-blind trial.<sup>32</sup> They studied 16 patients with CRPS I or II with three different levels of lidocaine infusion (1, 2, and 3 mcg/ml and placebo infusion) — during which the patients underwent spontaneous and evoked pain scores and detailed quantitative psychophysical testing. During the lidocaine (but not placebo) infusion, the patients showed evidence of a decrease in pain response to cold stimuli, and a decreased response to cold or touch allodynia in previously allodynic areas, and a decrease in spontaneous pain (but only at the highest serum infusion level). Thus, the predominant effect was decreased pain in response to cool stimuli more so than with mechanical or spontaneous pain. There was no effect on pain induced by punctate stimuli (level 2 evidence for short-term decrease in pain response to IV lidocaine infusion).

IV phentolamine infusion has been used largely as a diagnostic tool to differentiate SIP from SMP. These techniques have fallen out of favor and are lacking evidence of efficacy.

## OTHER (BRACHIAL PLEXUS/SPINAL BLOCKS-INFUSIONS) BLOCKS

There are numerous case reports of the use of brachial plexus blockade in the literature. Indications for continuous brachial plexus infusion include: perioperative posttrauma and postoperative pain relief, vascular compromise, intractable pain from CRPS I and II, and phantom limb pain. The brachial plexus is an ideal location for a continuous regional technique because of its well-defined perivascular compartment and the close approximation of the large number of nerves supplying the upper extremity. Catheters have been kept in place in the same position for as long as 3 weeks (level 4 evidence).<sup>33</sup> The brachial plexus catheter may be connected to a constant infusion of local anesthetic, opioid, clonidine, and other agents. Sympatholysis can still be maintained for up to 2 to 3 weeks with 0.1 to 0.2% ropivacaine in a reliably anchored catheter (level 4 evidence).<sup>34</sup>

Wang et al reported placement of an axillary catheter in a patient with severe CRPS II 30 days post carpal tunnel release (level 4 evidence).<sup>35</sup> These authors started with a concentration of bupivacaine of 0.1% at 2.5 ml/hour and noted a dense motor and sensory block with excellent analgesia. Within 1 day, they decreased the infusion to 0.05% bupivacaine, stopped the basal infusion, and allowed a 1 ml patient-controlled dose every 15 minutes. The patient had continued good analgesia with resolution of the motor block allowing active motion physical therapy, with the catheter left in place for 1 week.

The complications of a continuous brachial plexus infusion are similar to those of a brachial plexus block plus the infection risks of a long-term catheter. These include bleeding, infection, intravascular injection, intrathecal injection, pneumothorax, and phrenic nerve paralysis.

Epidural infusions are relatively straightforward to initiate, and allow one to vary local anesthetic concentration and infusion volume in order to titrate to desired effect. Other medications such as clonidine and/or opioids can be added to provide spinal analgesia and potentiate the degree of relief. The most commonly used combination of epidural medications today includes clonidine with/without bupivacaine. Opioids should be added if the pain relief is inadequate or if the local anesthetic concentration required to produce pain relief also prohibits ambulation or full participation in the physiotherapy program. The primary benefit of continuous regional analgesia is that one is able to effectively control the intense degree of relief and promote as aggressive a physical therapy program as can be tolerated. Furthermore, with patient-activated bolus programming, these continuous regional techniques allow patients to self-administer small boluses for optimal analgesia as the pain levels dictate. For example, after a strenuous exercise program which may elevate pain, swelling, or allodynia, patients have ready access to improved relief simply by self-administering extra doses of medication within certain preprogrammed parameters. The effectiveness of epidural analgesia for the treatment of CRPS has been borne out by several studies (see Table 2).

Rauck et al<sup>13</sup> did an excellent randomized, blinded, placebo-controlled trial utilizing epidural clonidine. They randomized 26 patients with CRPS to receive daily epidural infusions (for 3 consecutive days) of clonidine 300 or 600 mcg, or placebo. If patients responded to the clonidine with analgesia (and did not respond to placebo), they were placed on an open-label infusion for a mean of 32 days at a mean dose of 32 mcg/hour. All patients had “good relief” with both the 300 and 700 microgram dose. Of the 26 patients, 19 elected to receive continuous infusions of clonidine for an average of 43 days with an average dose of  $32 \pm 6$  micrograms per hour. Seventeen of 19 patients had statistically significant improvement in pain (level 2 evidence). Side effects were dizziness, dry mouth, mouth sores, and nausea. Six of 19 patients developed catheter related infection, and one developed meningitis (level 2 evidence).<sup>13</sup>

Cooper et al<sup>36</sup> studied 14 patients in a prospective open label trial and demonstrated improved pain relief and range of motion in patients receiving an epidural bupivacaine-opioid mixture for an average of 4 days (level 3 evidence).<sup>36</sup> Thirteen of 14 patients had significant improvement, with 11 of the 14 achieving “resolution of their CRPS” (at least at the end of the trial) with no activity restrictions. König<sup>37</sup> studied 26 patients using continuous cervical epidural analgesia of bupivacaine (0.25%) for 7 days coupled with physical therapy (level 3 evidence).<sup>37</sup> Eighty-three percent of patients had “improvement in pain.” Edema, sweating abnormalities, and dysfunction of the hand responded particularly well. Sixty-three percent of patients considered their condition to be acceptable whereas only 8% were completely pain free. Reduction in use of pain medications was also noted. Finally, Buchheit and Crews describe a single case report where continuous epidural infusion markedly improved range of motion (level 4 evidence).<sup>38</sup>

The reported rates of infection in epidural catheters used to treat CRPS are as high as 31%.<sup>13</sup> Thus, epidural catheters that are meant for longer-term use should be performed as minor surgical procedures requiring standard surgical sterility techniques. Catheters should be tunneled away from the midline entrance point in the spine to minimize the colonization by bacteria that is inherently a greater risk with extended duration infusions. In spite of precautions, CRPS patients may be predisposed to an increased chance of infection. Standard catheter dressings such as those required for extended central venous catheters should be followed. Dressings should be changed weekly in meticulous sterile fashion as with a central venous line. A Du Pen’s epidural catheter (CR Bard, Inc, Murray Hill, NJ, USA) has a built-in antimicrobial cuff that may lead to lower infection rates. The hallmarks of an epidural abscess include the triad of back pain, sensorimotor loss, and loss of bowel and bladder function. Epidural abscesses usually have some earlier prodromal symptoms such as fever, neck pain, or photophobia. Careful attention to early symptoms is paramount for early diagnosis. A previous study has demonstrated a catheter-related infection rate of 19 out of 350 patients. All of these patients were treated with antibiotics and catheter removal, and none required surgical intervention.<sup>39</sup>

Intrathecal analgesia has been less well studied, with Lundborg reporting a series of three patients with highly refractory CRPS who did not have a good clinical response to intrathecal bupivacaine. In spite of initial analgesia, all of these patients had progression of their CRPS (level 4 evidence).<sup>40</sup> In a small subset of patients (n=7) with refractory CRPS and severe dystonia, van Hilten et al<sup>41</sup> had good outcomes of analgesia with functional restoration using intrathecal baclofen injected in a double-blind fashion, followed by intrathecal infusion (level 2 evidence for IT baclofen in *dystonic* CRPS).

Many have adopted epidural infusion techniques as next line therapy for patients failing intermittent blocks with strong evidence for efficacy of epidural clonidine. This procedure is technically easy to perform, with level 2 evidence supporting epidural clonidine infusion as outlined above. Some centers have utilized the plexus infusions described above, but the epidural techniques are more common. The main drawback to these infusion techniques is the rate of infection, which remains to be defined by further prospective study on infusion techniques in CRPS patients. Intrathecal baclofen infusion (via implanted pump) is advised in patients with a dystonic component to their CRPS, with level 2 evidence supporting this treatment. Intrathecal infusion for CRPS without dystonia has only limited supporting literature.

## NEUROLYTIC SYMPATHETIC BLOCKS (RF/ALCOHOL-PHENOL)

Surgical sympathectomy has been utilized to treat SMP and other hyperactive sympathetic syndromes (including hyperhidrosis and Raynaud's phenomenon among others) since 1889 and historically was an important treatment for RSD.<sup>4,42</sup> These surgical techniques were performed in an open operation, but recently both upper and lower extremity sympathectomy are being done via endoscopy with a minimally invasive technique, as initially described in the 1950s and recently "rediscovered" in a small prospective case series (level 4 evidence).<sup>5</sup> More recently, radiofrequency techniques have been described in a large case series (level 4 evidence).<sup>43</sup>

Kim et al<sup>42</sup> reviewed the available literature for surgical sympathectomy and found an initial failure rate of up to 35%, usually ascribed to poor patient selection.<sup>42</sup> Other possibilities for failure to achieve analgesia include incorrect diagnosis, inadequate resection, reinnervation, and contralateral innervation. In light of the difficulty of clinically assessing adequacy of sympathetic blockade based on clinical criterion, it is easy to understand the difficulty in assessing the local anesthetic sympathetic block's predictive value for surgical sympathectomy.<sup>16</sup> The ablative sympathectomy techniques have been available for many years, but as yet, no high-level evidence exists to support their widespread use.

Another significant problem with ablative sympathectomy is recurrence of former symptoms and "post sympathectomy neuralgia" 6 months to 2 years post sympathectomy. These postablative neuralgic syndromes may respond to re-resection or spinal cord stimulation (level 3 evidence for SCS).<sup>44</sup> The reported incidence of this clinical phenomenon is up to 44% in a series of open sympathectomy for causalgia.<sup>45</sup>

Wilkinson<sup>43</sup> reports the largest series of percutaneous Radio Frequency (RF) lesioning of the thoracic T-2 distribution sympathetic outflow (RF sympathectomy), with over 350 procedures performed with 86% signs of sustained sympathectomy at 3-year follow-up, without any assessment of clinical analgesic or functional outcomes (level 3 evidence for *interruption of sympathetic activity* in a prolonged fashion with RF techniques).<sup>43</sup> Wilkinson reports difficulty with lumbar percutaneous RF techniques due to variability of the lumbar anatomy versus the thoracic ganglion. He also reports a low rate of postprocedure neuralgic syndromes (around 5%), although this is recorded in an unpublished data format within a book chapter.<sup>42</sup> This author could find no published data yet on pulsed RF sympathetic ganglion techniques.

Sympathetic ablation techniques have been advocated for many years, mainly by surgeons. In general, neurodestructive techniques to treat chronic pain syndromes are not currently recommended due to questionable outcomes, and the potential risk for developing deafferentation syndromes or "post sympathectomy neuralgia." The same holds true for neurolytic blocks utilizing alcohol or phenol, which have largely been relegated to the terminally ill. The radiofrequency ablative techniques are much more controllable than neurolytic solution injections, and less invasive than surgical ablation. Preliminary reports in the form of case series are promising, but the exact role of RF ablation sympathectomy versus periodic blockade versus neurostimulation is uncertain.

## NEUROSTIMULATION

Research of high quality regarding spinal cord stimulation (SCS) and CRPS is limited, but existing data is positive in terms of pain reduction, quality of life, analgesic usage, and function.

Kemler et al<sup>46</sup> published a prospective, randomized, comparative trial to compare SCS versus conservative therapy for CRPS. Patients with a 6 month history of CRPS of the upper extremities were randomized to undergo trial SCS (and implant if successful) plus physiotherapy versus physiotherapy alone. In this study, 36 patients were assigned to receive a physical therapy program together with SCS, whereas 18 patients were assigned to receive therapy alone. In 24 of the 36 patients randomized to SCS, the trial was successful and permanent implantation was performed. At a 6-month follow-up assessment, the patients in the SCS group had a significant reduction in pain, and a significant percentage graded the global perceived effect as improved. However, there were no clinically significant improvements in functional status. The authors concluded that in the short-term, SCS reduces pain and improves the quality of life for patients with CRPS involving the upper extremities. The improvement in pain scores, global perceived effect, and overall health-related quality of life, although modest, were significant and sustained for 2 years follow-up as published in a subsequent manuscript.<sup>47</sup> Further analysis of this patient subgroup has revealed no difference in outcomes for cervical versus lumbar SCS in terms of effectiveness or complication rate.<sup>48</sup>

Several important case series have been published on the use of neurostimulation in the treatment of CRPS. Calvillo<sup>49</sup> reported a series of 36 patients with advanced stages of CRPS (at least 2 years duration) who had undergone successful SCS trial (>50% reduction of pain).<sup>49</sup> They were treated with either SCS, or peripheral nerve stimulation, and in some cases with both modalities. Thirty-six months after implantation, the reported pain measured on visual analogue scales was an average of 53% better, and this change was statistically significant. Analgesic consumption decreased in the majority of patients. Forty-one percent of patients had returned to work (on modified duty). The authors concluded that in late stages of CRPS, neurostimulation (with SCS or PNS) is a reasonable option when alternative therapies have failed. Two groups have critically reviewed these and other studies and case report literature and concluded that there is moderate evidence that SCS is effective in treating CRPS related pain.<sup>50,51</sup>

## CONCLUSIONS

With a new understanding of CRPS as encompassing *both* SIP and SMP in varying degrees among different patients, sympatholysis remains an important diagnostic (SMP vs SIP) and therapeutic modality (in the SMP subgroup). Because of the considerable difficulty in “clinically assessing” the successful sympathetic block, and because “clinically successful” blocks provide varying degrees of sympatholysis,<sup>16</sup> the role of local anesthetic injection sympathetic blockade versus IVRA, IV, or epidural sympatholysis is unknown and largely based on local practice patterns. Additionally, with the notable paucity of good quality supportive outcomes studies, the clinician is left to utilize these blocks or sympathectomy-inducing infusions within the context of a broad algorithm of interdisciplinary treatment, while awaiting further pathophysiological data and outcomes research to guide our practice to the most beneficial treatments.

The decision to proceed with RF ablative techniques versus other nondestructive alternatives is a complex one, with less evidence for the ablative versus augmentative treatments. Due to the adverse long-term post sympathectomy syndromes, this author currently recommends against surgical ablative sympathectomy. Future studies may expand on the role of pulsed RF (cold RF) techniques or such unstudied techniques as cryosurgery as alternative therapies to treat SMP.

Our recommended strategy (and tactic) is to use interventional treatments for CRPS patients who are having difficulty either starting or progressing in the functional restoration/interdisciplinary algorithm. If patients are not progressing because of high pain levels (especially associated with autonomic dysfunction), then a stepwise progression — from the less invasive blocks, to infusions or catheter infusion therapies, and ultimately perhaps to neurostimulation — is recommended in order to facilitate the patient's functional improvement and pain control. One suggested algorithm developed by an expert panel for the integrated use of these procedures is shown in Figure 1 and has been previously published.<sup>1</sup>

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**TABLE 1. POOLED ANALYSIS OF AVAILABLE LOCAL ANESTHETIC SYMPATHETIC NERVE BLOCK STUDIES\***

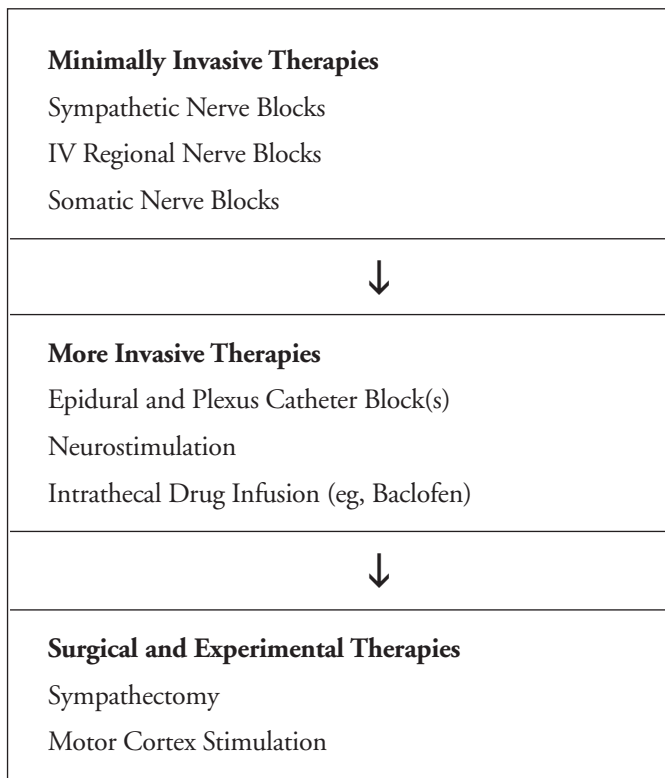
\*(Adapted from <sup>17</sup>.)

Overall N	Block Technical Success Graded (%)	% Prospective Evaluation	Range of Follow-up	Range of Pain Relief Duration	Range of Number of Blocks	Pain Relief Response (%)		
						Absent	Partial	Full
N=454	17%	23%	48h-8yr	3h-8yr	1-25	32%	41%	29%

**TABLE 2. CONTINUOUS EPIDURAL INFUSIONS FOR CRPS**

Author	# of Pts	Infusion Mixture	Results	Complication
Cooper et al 1989 <sup>36</sup>	14	Bupivacaine-opioid	Improved pain relief and ROM 13/14	None
Konig et al 1995 <sup>37</sup>	26	Bupivacaine .25%	83% improved pain 63% acceptable reduced opioid use	Catheter site infection 8% Catheter dislodgement 23%
Rauck et al 1993 <sup>13</sup>	19	Clonidine	Improved pain	Dizziness 5/19 Nausea 5/19 • Mouth sores 4/19 Dry mouth 3/19 • Infections 6/19
Buchheit et al 2000 <sup>38</sup>	Single case report	Bupivacaine .125% Clonidine .0005%	Improved ROM	None

**Figure 1. Interventional pain treatment algorithm for CRPS\***



Inadequate or partial response to any given therapy should lead to a stepwise progression down through these modalities (moving from less to more invasive) in conjunction with other noninterventional treatments.

\* Adapted from <sup>1</sup>