

# Management of Pediatric Patients With Complex Regional Pain Syndrome

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**Abstract:** This review summarizes current information about diagnosis and treatment of complex regional pain syndrome (CRPS) in children. Although it has been widely held that CRPS in children is intrinsically different from adults, there appear to be relatively few differences. However, there is a marked preponderance of lower extremity cases in children. Historically, psychological factors have been invoked to explain the genesis and persistence of CRPS in children, but the evidence is not compelling. Treatment outcome studies are limited but indicate that children generally respond to a primary focus on physical therapy. Multidisciplinary treatment reports are particularly encouraging. The general perception that children have a milder course may relate to the potentially greater willingness of children to actively participate in appropriately targeted treatment rather than to innate differences in the disease process itself. Recurrence rates appear higher than in adults, but response to reinitiation of treatment seems to proceed efficiently. Clinical judgment dictates the extent of medication or interventional therapy added to the treatment to facilitate rehabilitation. In many ways, the approach to the treatment of children mirrors that of adults, with perhaps greater restraint in the use of medications and invasive procedures. The rehabilitation of children with CRPS, like that of adults with CRPS, needs further rigorous investigation.

**Key Words:** complex regional pain syndrome, pediatric

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## DEMOGRAPHICS

In children less than 18 years of age, complex regional pain syndrome (CRPS) type 1 develops most commonly in girls, with the incidence rising at or just before puberty.<sup>1–5</sup> The lower extremity is more commonly affected than the upper, with a ratio of about 5:1. Type 1 CRPS seems to be more common among Caucasian children. I have noted this association in my practice at both Children's Hospital, Boston, and at the Mayo Clinic, Rochester. To exclude sampling bias, physicians at Children's Memorial Hospital in Chicago and Children's

Hospital Medical Center in Cincinnati were also polled (personal report from S. Suresh, Children's Memorial Hospital, Chicago, IL, and K. Goldschneider, Children's Hospital Medical Center, Cincinnati, OH). Although these hospitals have a substantial proportion of minority patients, the same association was seen there. Bernstein et al<sup>4</sup> also reported this association: 18 of 23 patients in their report were Caucasian, 4 Hispanic, and 1 black. This may not be unique to children, however as Allen et al reported a similar distribution in adult patients: 91% (107 of 118) of their population was Caucasian.<sup>6</sup>

CRPS type 2 is found with roughly equal incidence in both boys and girls and has been noted in children as young as 3 years of age.<sup>7,8</sup> Interestingly, however, even though brachial plexus injury during delivery is common and can lead to longstanding motor weakness, neonates with Erb's palsy do not generally develop pain in the extremity.

## DIAGNOSIS

The diagnosis of CRPS remains a clinical one based on appropriate findings in the history and physical examination. Pain, particularly with allodynia, and signs of autonomic instability either historically or on examination are required to make this diagnosis. The pain should be out of proportion to the inciting event, if any, and is usually distally generalized in the extremity.<sup>9</sup> Pathologic processes that might explain the pain must be excluded. There are no laboratory tests that can absolutely confirm or exclude this diagnosis.

A group from Belgium including Herregods,<sup>10</sup> Franckx,<sup>11</sup> Chappel, and others has argued that disturbed vascular scintigraphy with increased pooling in the initial phase and hyperfixation on bone scintigraphy is necessary on bone scan to make the diagnosis of CRPS. In contrast, most other authors find that bone scans are quite nonspecific for the diagnosis of CRPS. Multiple authors have found that in patients meeting the clinical diagnosis, bone scan may show either hypofixation or hyperfixation or may be normal.<sup>3,5,12,13</sup> This is not to say that bone scans are not useful in working up the patient with signs and symptoms of CRPS; however, the primary utility is in ruling out some underlying orthopaedic abnormality that might be triggering the neurovascular changes rather than diagnosing CRPS.

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## TREATMENT

CRPS in pediatric patients has always been considered different from CRPS in adults. Early large series of CRPS (or reflex sympathetic dystrophy, as it was known at the time) suggested that the syndrome was extremely rare in children.<sup>14,15</sup> Sporadic early reports of children with CRPS first appeared in the 1970s. Several of these patients had spontaneous resolution.<sup>16,17</sup> This led to the suggestion that no treatment should be performed for children with CRPS. The rationale was that all treatments carry risks and side effects, and for a self-limited disease these should be avoided.<sup>17</sup> Other authors used treatment strategies very similar to those used in adults, including sympathetic blocks, antidepressants, vasodilators, steroids, and so forth, generally with complete resolution of the disease.<sup>15,17-19</sup> Between these two extremes was a group of authors recommending conservative treatment consisting primarily of physical therapy (PT) either with<sup>8,20</sup> or without<sup>4</sup> concomitant use of transcutaneous electrical nerve stimulation (TENS). The overall impression is that CRPS is more easily treated in children than in adults. This impression is challenged by later reports from Wilder et al,<sup>1</sup> Stanton et al,<sup>3</sup> and Greipp<sup>21,22</sup> showing that a percentage of children will have long-term pain and disability even with aggressive therapies such as sympathetic-chain catheters, and antidepressant and anticonvulsant medications.

### Physical Therapy

A recent report by Sherry et al<sup>5</sup> contradicts this pessimistic viewpoint. Using a program consisting exclusively of PT up to 6 hours per day, without any blocks or medications, they reported a cure rate of over 90%. These impressive results are similar to those Bernstein et al<sup>4</sup> reported for PT alone two decades earlier. Murray et al<sup>23</sup> also reported similar results using PT as the primary treatment modality: 40 of 46 patients resolved with intensive PT alone.

A major school of thought is that PT is the treatment modality that offers a chance for resolution of CRPS in either adults or children.<sup>24</sup> All other therapies, when used, should be prescribed with the goal of facilitating the basic PT regimen. From this hypothesis one would predict that more intensive PT would provide faster and more complete resolution of CRPS. Although nonrandomized trials of intensive PT by Sherry et al,<sup>5</sup> Murray et al,<sup>23</sup> and others would seem to support this, a recent prospective randomized trial by Lee et al<sup>25</sup> does not. In this study patients were assigned to once-weekly or three-times-weekly outpatient PT along with a baseline of weekly cognitive-behavioral sessions. Results for both groups were good, with pain scores decreasing to near zero and function improving, but no statistically significant difference was found between the two groups. This may have been limited by small sample size (13 per group) or because the actual amount of exercise performed may have been similar between the two groups. Curiously, the trend was for more complete resolution in the once-weekly group.

## TENS

TENS is a noninvasive physical modality that may provide excellent analgesia for some patients. It has been described in several case reports and series.<sup>1,26-32</sup> None of these series describe TENS as universally effective, and there are no prospective, blinded trials of efficacy. In view of the modest cost, generally high acceptance by children, and remarkable safety of this device, it is almost always worthwhile giving a trial of TENS as part of a multidisciplinary approach to CRPS.

### Biobehavioral and Psychological Treatments

Much has been written about psychological aspects of children with CRPS. Authors have invoked psychological contributions to the disease since the earliest case reports of CRPS in children appeared. Carron and McCue, in their 1972 description of a child with CRPS, stated that they made "the usual referral to psychiatry and for sympathetic blocks."<sup>15</sup> Some authors have even presumed that CRPS is entirely a psychological or psychosomatic disease process.<sup>33</sup> Presumably they are confused because CRPS crosses dermatomes and areas of innervation by single nerves to form a distally generalized stocking-and-glove distribution. The marked allodynia and pain far out of proportion to the original inciting injury, if any, have also caused many practitioners to question whether CRPS has an organic basis or is of purely psychological origin.

There is scarce evidence that children with CRPS are psychologically unique. Sherry and Weisman<sup>34</sup> studied 21 families of children with CRPS. These were generally high-achieving, compliant children. They found that in virtually all cases there was significant parental enmeshment with the patient. Beyond that, they found that multiple different stressors were present in these children, including marital conflict between the parents ( $n = 12$ ), significant school problems ( $n = 13$ ), and sexual abuse ( $n = 4$ ). Testing revealed no major psychopathology, except for one child who scored high in somatization. Sherry and Weisman suggested that CRPS is frequently a stress-related disease, and the therapeutic approach must take these psychosocial factors into account. One difficulty with this study is that appropriate control groups were not tested with equal thoroughness. Children with new-onset arthritis were compared in terms of global assessment, but the other psychological tests were not reported for this control group. A healthy control group was not included.

A case series by Brommel et al<sup>35</sup> also found psychological dysfunction in children with CRPS. They concluded that the despair of the patients about their reflex sympathetic dystrophy expressed unsolved fears of early childhood. Again, no control groups were studied. Stanton et al,<sup>3</sup> in reviewing a series of patients with CRPS, noted that 83% of the patients given psychological evaluations had "significant emotional dysfunction." This was not further defined, although they also noted a great deal of stress in the lives of the patients. In contrast, Vieyra et al<sup>36</sup> performed a preliminary study comparing

patients with CRPS to children with migraine headaches and 21 normal controls. Contrary to expectations, no differences in family functioning were found among the three groups. Unfortunately, this work was never published in a peer-reviewed journal. A literature review by Lynch<sup>37</sup> in 1992 and recent prospective psychological studies of CRPS in adults also support that these patients are not psychologically unique from others with chronic pain.<sup>38,39</sup>

In isolated cases, psychological factors may indeed have a predominant role in the etiology of CRPS. Jaworowski et al<sup>40</sup> reported CRPS in a 12-year-old who developed simultaneously a conversion disorder; her identical twin also developed an identical conversion disorder.

Whether or not psychological dysfunction exists prior to the onset of CRPS, psychological, cognitive, and behavioral strategies are often used as part of the treatment of children with CRPS. Case reports of successful treatment of CRPS with cognitive and behavioral strategies began to appear in the 1980s.<sup>41,42</sup> There are no prospective placebo-controlled trials of cognitive and behavioral therapies in the treatment of CRPS, either in adults or children. Their use is extrapolated from case reports and prospective series for other pain states, notably headache.<sup>43,44</sup> Wilder et al<sup>1</sup> reported that 57% of their patients who received such training benefited from it and continued to use this treatment modality. Stanton et al,<sup>3</sup> however, found that psychological interventions were not consistently effective. This was felt to be due to the short time for interactions with the therapist during the patient's inpatient admission. Lee et al<sup>25</sup> used cognitive and behavioral therapy as part of their baseline treatment of CRPS patients who were randomized to receive one or three sessions per week of PT. Compliance with attending the sessions was good and overall results were good, but the specific effect of the cognitive and behavioral treatments was not broken out. Sherry et al<sup>5</sup> did not use formal cognitive or behavioral treatments in his series of 103 patients treated with intensive PT, but they did refer 77% for psychological counseling, either individual or family. The results from the counseling were not measured or studied.

### Sympathetic Blocks

In previous years many authors have equated sympathetically mediated pain with CRPS. During the 1993 consensus conference that eventually led to the new taxonomy of CRPS, there was widespread agreement that the pain of CRPS could be sympathetically maintained, sympathetically independent, or some combination of both that could change over time.<sup>45</sup> Sympathetic blocks may help define the proportion of pain that is sympathetically mediated at that time and may be of therapeutic benefit, but they do not confirm or revoke the diagnosis of CRPS. When sympathetic blocks are used in the treatment of childhood CRPS, several authors have proposed the use of indwelling catheters rather than repeated single injections.<sup>1,25,46</sup> There are several reasons

to prefer this technique. First, accurate placement of a lumbar sympathetic block is facilitated by use of fluoroscopy. Minimizing radiation exposure is appropriate for children. Second, many children and adolescents require heavy sedation or a brief anesthetic for the placement of these blocks. Minimizing the number of anesthetics required is also useful. Third, the goal of the sympathetic block is not to "treat" the CRPS per se, but rather to provide adequate pain relief that the patient can effectively engage in PT. An indwelling sympathetic-chain catheter, when effective, provides continuous pain relief without motor or sensory dysfunction and can be highly effective in allowing PT to proceed. These patients are generally hospitalized. Indeed, one advantage of the indwelling catheter is that it mandates hospitalization, which may allow more intensive PT than is available on an outpatient basis. Single-shot sympathetic blocks need to be coordinated with the PT sessions so that the patient is pain-free during the sessions. Indwelling epidural catheters, although often effective in relieving the pain, cause sufficient motor and/or sensory block that the patient cannot effectively participate in PT. This may be counterproductive, as any immobilization of the limb appears to worsen CRPS. Use of clonidine or opioids along with low concentrations of local anesthetic in the epidural catheters may avoid this problem, but this may not provide adequate analgesia. Several authors who emphasize intensive PT as the sole treatment modality for childhood CRPS actually recommend against the use of sympathetic blocks.<sup>3,5,25</sup> They have reported success motivating their patients to participate in PT despite ongoing pain and allodynia. Others<sup>1,25,47</sup> have used blocks to improve compliance in patients unwilling or unable to participate in PT secondary to pain. At present there are no prospective trials directly comparing outcomes in pediatric CRPS with or without sympathetic or epidural blockade.

### Medications

There are also no prospective randomized clinical trials of any medications in the treatment of CRPS in children. Case reports and case series have reported success with tricyclic and other antidepressants,<sup>1</sup> anti-convulsants (particularly gabapentin),<sup>48,49</sup> steroids<sup>50-54</sup> (either systemically or as part of an intravenous regional technique),<sup>55</sup> nonsteroidal anti-inflammatory agents,<sup>56</sup> and opioids, both systemic and neuraxial. A good deal of controversy exists about drug therapy for this condition. Many authors have found steroids to be of no benefit.<sup>1,4,57</sup> Those who stress the value of intensive PT suggest that no medications are appropriate.<sup>5,23</sup> The rationale is that all medications may have side effects and the potential for morbidity. As they are not necessary in the view of these authors, they should be avoided. Sherry et al stopped all medications at the start of the PT program.<sup>5</sup> A direct comparison of intensive PT with or without any of these medications is lacking.

## Neurosurgical Techniques

A few children with CRPS fail to respond to multiple treatment approaches, including the stepwise multidisciplinary approach used by Wilder et al<sup>1</sup> and Lee et al<sup>25</sup> and the intensive PT approach used by Sherry et al.<sup>5</sup> These children and their parents will often seek multiple medical opinions and undergo increasingly invasive and dangerous procedures in their quest for pain relief. Two types of neurosurgical procedures have been used in these patients: spinal cord stimulation (SCS) and sympathectomy. There is moderate evidence supporting the use of SCS in the treatment of CRPS in adults. Retrospective series by Kumar et al<sup>58</sup> and Kemler et al<sup>59</sup> and a later prospective series by Kemler et al<sup>60</sup> all show efficacy in terms of sustained pain reduction of modest proportions. Pain thresholds are not changed by SCS.<sup>61</sup> No series of children undergoing SCS have been reported, although I know of at least a half-dozen children who have undergone SCS for CRPS. Results have been mixed, ranging from modest improvement in pain and function to a worsening of pain, with explantation of the system. SCS has an advantage over sympathectomy in that it is nondestructive and completely reversible.

Sympathectomy, either chemical or surgical, has been reported in children with CRPS. Disadvantages of this procedure include the fact that it is appropriate only for the sympathetically mediated portion of the patient's pain, that it is irreversible and may cause sympathalgia, and that long-term physiologic effects of lumbar sympathectomy on adolescent girls are not well characterized. In a mixed series of adults and children, Bandyk and Johnson<sup>62</sup> reported an initial 10% failure rate. With 30-month follow-up, long-term results showed a reduction in pain relief overall to 25% excellent relief (pain scores < 3 of 10), and 50% with pain that was moderately reduced from before the block. Wilder et al<sup>1</sup> reserved the use of sympathectomy for patients with impending loss of function from cellulitis complicating massive peripheral edema. The three patients undergoing these procedures did not have improvement in pain scores despite improvement in circulation and edema.

## Complementary and Alternative Medicine

Randomized, blinded trials showing the efficacy of acupuncture are also lacking in CRPS. One such study has been performed, but there was improvement in both groups, with no statistical difference between groups.<sup>63</sup> There are studies showing a surprisingly high acceptance rate for acupuncture therapy among children.<sup>64,65</sup> There are also case reports of benefit to this therapy.<sup>66</sup> It is rational to think that acupuncture, by its mechanisms of raising endogenous opioids and acting as a counter-stimulant to "close the gate" on spinal cord transmission of pain signals, might be of benefit in this disorder. Well-blinded studies are difficult to design, however, so obtaining definitive proof of efficacy may be slow in coming.

Although many patients may have used herbal remedies and nutritional supplements, there are no

studies or even case reports of their efficacy. Most herbal remedies contain active biochemicals. They may indeed benefit some patients, but they may also have significant interactions with any medications that might be prescribed, and may have toxicity in their own right.

## CONCLUSIONS

CRPS in children has been widely held to be intrinsically different from that in adults. This has been based on both demographics and a perception that children may have a milder course or a better response to conservative treatments. Other than the marked preponderance of lower extremity CRPS in children and adolescents, the demographics do not seem all that different for children than adults. A female preponderance exists for both groups. Both appear to have Caucasian predominance. Psychological factors are often invoked in pediatric CRPS, including enmeshment of the patient and parents and a degree of overachievement. Although this certainly may play a predominant role in some cases, the available evidence is not compelling that children with CRPS are unique compared with either other children with chronic pain or adults with CRPS. Finally, as regards the perception that children have an easier course than adults do, the evidence is not strong. Certainly, several series have reported children responding to courses of intensive PT alone. Nonetheless, the consensus is that PT is the definitive treatment of adults with CRPS as well as children. I have been unable to locate any series of intensive (5–6 hours per day) PT programs for adult patients analogous to that reported by Sherry et al.<sup>5</sup> Series using less-intense PT, as reported by Wilder et al<sup>1</sup> or Lee et al,<sup>25</sup> give results similar to a stepwise multidisciplinary treatment plan in adults.<sup>67</sup> The apparent mildness of pediatric CRPS may be due to a greater willingness of children to actively participate in appropriate PT more than to an innate difference in the disease process itself.

The potential for recurrence of CRPS is often of great concern to children with this syndrome and to their parents. Studies have shown a fairly high rate of recurrence in the same limb after successful treatment or spread to another limb concurrent with the initial diagnosis.<sup>5,25</sup> Recurrence occurred in approximately 30%<sup>5</sup> to 50%<sup>25</sup> of patients, a much higher rate than the rate of 1.8% per patient-year reported for adults.<sup>68</sup> Although recurrence is common, it generally seems to respond more readily to physical therapy and related treatments than the initial episode.<sup>5,25</sup> A case report by Tong and Nelson<sup>48</sup> illustrated that for some children the recurrent bouts of CRPS may be as severe as or even more severe than the original.

In summary, although not definitively proven, PT leading to active normal use of the involved extremity is generally held to be the single most effective therapy in the treatment of CRPS. Children may be willing to participate in PT, despite the associated pain, with proper motivation. In general, however, the clinician's job is to

help provide adequate analgesia to speed progress in PT. A stepwise, multidisciplinary approach is generally in the patient's best interest, starting with minimally invasive modalities such as TENS and biobehavioral pain management techniques. Acupuncture may be useful at this point, too, if there is a practitioner available in the community who has experience working with children. If needed, medications with a proven track record in neuropathic pain management can be added, such as the tricyclic antidepressants (nortriptyline or amitriptyline) or anticonvulsants (gabapentin and others). Children taking these medications need to be monitored carefully for side effects to optimize the risk/benefit ratio. Sympathetic blocks can be useful to accelerate recovery; they are unlikely to be effective monotherapy for CRPS, but they do have a role as a way to help a patient work more actively in an ongoing PT program. Using the above approach, most patients will have an excellent response. For those who cannot sustain improvement despite an ongoing exercise program, neurosurgical techniques such as SCS or, in highly selected cases, sympathectomy may be useful. These techniques are not guarantees of success, and they should be used only as a part of a multidisciplinary program stressing exercise and rehabilitation.

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